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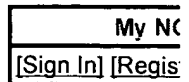
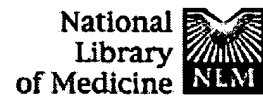
Detergents containing either a cholic acid, a deoxycholic acid, or an octanoic acid-like hydrophobic moiety and a bisgluconamidopropyl polar group were synthesized. Extinction coefficients, partial specific volumes, critical micelle concentrations, and aggregation numbers were determined for each of the detergents. The two bile acid derivatives are capable of solubilizing functional opiate receptor, while the octanoic acid derivative is not.

PMID: 6869837 [PubMed - indexed for MEDLINE]

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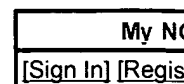
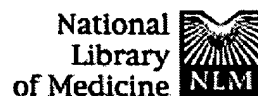
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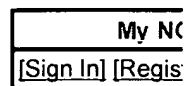
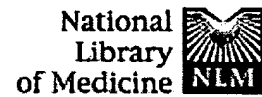
Hjelmeland LM, Nebert DW, Osborne JC Jr.

The syntheses of four new sulfobetaine derivatives of bile salts are presented, along with a general set of criteria for useful detergents in membrane biochemistry. Physical properties including the critical micelle concentration, aggregation number, partial specific volume, critical micellar temperature, uv-vis spectrum, and circular dichroism spectrum are examined for the new compounds. To examine the interaction of this class of compounds with macromolecules, one of these (CHAPS) was further studied. Circular dichroism spectra of apolipoprotein C-III2 were measured in the presence of varying concentrations of CHAPS to determine the effect of this compound on secondary structure. Gel-exclusion chromatography and sedimentation equilibrium studies of cytochrome P-450 in the presence of CHAPS were also performed to establish the ability of this detergent to disaggregate cytochrome P-450 to a monomeric/dimeric state.

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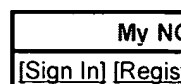
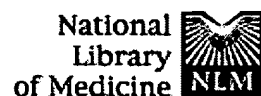
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A nondenaturing zwitterionic detergent for membrane biochemistry: design and synthesis.

Hjelmeland LM.

The synthesis and evaluation of a new detergent that is a zwitterionic derivative of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

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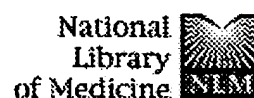
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
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
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













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Identification of the multicatalytic enzyme as a possible gamma-secretase for the amyloid precursor protein.

Mundy DL.

Department of Neurology, Baylor College of Medicine, Houston, TX 77030.

One of the main components of the senile plaques in brain tissue from patients with Alzheimer's disease is the beta-amyloid peptide. This peptide is proteolytically cleaved from the amyloid precursor protein by the action of at least two proteases, a beta-secretase which generates the N-terminus and a gamma-secretase which generates the C-terminus. Neither of these proteases have been identified. To identify proteases that are candidates for the gamma-secretase we synthesized a fluorescent peptide substrate containing the amino acids comprising the C-terminus of the longest beta-amyloid peptide identified. This substrate is hydrolyzed by a single activity in homogenates from both cells and brain tissue and we have demonstrated that this activity is the multicatalytic enzyme proteasome. Furthermore, using specific inhibitors, we have demonstrated that the fluorescent substrate is hydrolyzed by a chymotrypsin-like activity of the multicatalytic enzyme.

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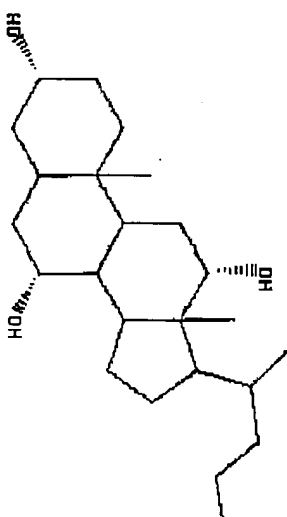
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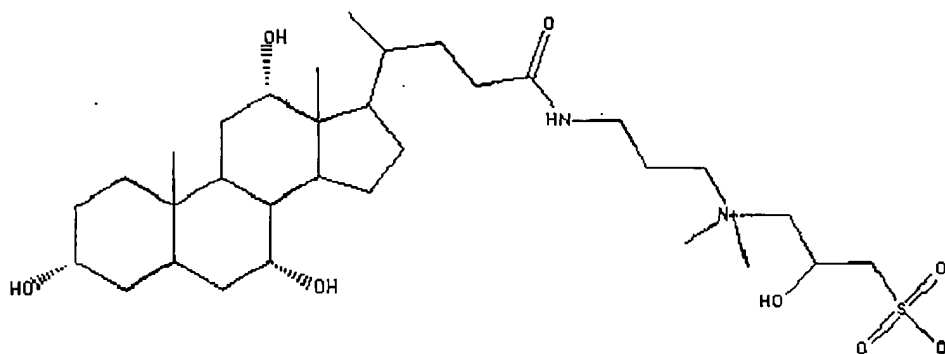
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Biochemical and Biophysical Research Communications

Volume 204, Issue 1 , 15 October 1994, Pages 333-341

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Regular Article

Identification of the Multicatalytic Enzyme as a Possible γ -Secretase for the Amyloid Precursor Protein

Mundy D. I.

Baylor Coll Med, Dept Neurol, Houston, TX 77030, USA

Available online 29 April 2002.

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One of the main components of the senile plaques in brain tissue from patients with Alzheimer's disease is the β -amyloid peptide. This peptide is proteolytically cleaved from the amyloid precursor protein

by the action of at least two proteases, a β -secretase which generates the N-terminus and a γ -secretase which generates the C-terminus. Neither of these proteases have been identified. To identify proteases that are candidates for the γ -secretase we synthesized a small fluorescent peptide substrate containing the amino acids comprising the C-terminus of the longest β -amyloid peptide identified. This substrate is hydrolyzed by a single activity in homogenates from both cells and brain tissue and we have demonstrated that this activity is the multicatalytic enzyme or proteasome. Furthermore, using specific inhibitors, we have demonstrated that the fluorescent substrate is hydrolyzed by the chymotrypsin-like activity of the multicatalytic enzyme.

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SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
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CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

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CI MAN
SR CA
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DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 123:260401 CA
TITLE: Calculation of partial specific volumes of detergents and lipids
AUTHOR(S): Durchschlag, Helmut; Zipper, Peter
CORPORATE SOURCE: Institute of Biophysics and Physical Biochemistry, University of Regensburg, Regensburg, D-93040, Germany
SOURCE: Comunicaciones presentadas a las Jornadas del Comité Español de la Detergencia (1995), 26, 275-92
CODEN: CJCDD7; ISSN: 0212-7466
PUBLISHER: Comité Español de la Detergencia, Tensioactivos y Afines
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 46-2 (Surface Active Agents and Detergents)

ABSTRACT:

Volumetric properties of surfactants are required for the application of various techniques. As an alternative approach to densimetric expts., ab initio calcn. of partial vols. may be performed. Our previously established calcn. procedure is based on some kind of additivity principle, using the partial molar volume increments for the constituent atoms, ions and/or groups, and some special increments/decrements for covolume, ring formation and ionization. The validity of this approach was also confirmed by a systematic comparison of exptl. and calculated values of different classes of detergents and lipids. The majority of vols. calculated for the monomeric state are already within a range of $\pm 3\%$, if compared with the exptl. values which in most cases, however, were determined above critical micelle concentration. Applying appropriate volume increments for micellization in certain cases, the volume changes due to the formation of supramol. structures can be taken into account. This enhances the accuracy of predicted vols. of micellar surfactants considerably ($\pm 2\%$ in 80% of the cases).

SUPPL. TERM: partial specific vol detergent lipid calcn
INDEX TERM: Detergents
(calcn. of partial sp. vols. of detergents and lipids)
INDEX TERM: Lipids, properties
ROLE: PRP (Properties)
(calcn. of partial sp. vols. of detergents and lipids)
INDEX TERM: Specific volume
(partial, calcn. of partial sp. vols. of detergents and lipids)
INDEX TERM: 9016-45-9, Poly(oxy-1,2-ethanediyl), α -(nonylphenyl)- ω -hydroxy-
ROLE: PRP (Properties)
(Arkopal 9 or Surfonic N-95 or Triton N-101 or Arkopal 13; calcn. of partial sp. vols. of detergents and lipids)
INDEX TERM: 9002-92-0, Polyoxyethylene monododecyl ether
ROLE: PRP (Properties)
(Atlas G 2127 or Lubrol PX or Nopalcol 6L; calcn. of partial sp. vols. of detergents and lipids)
INDEX TERM: 53-60-1, Promazine hydrochloride 56-81-5, Glycerol,

properties 57-09-0, Hexadecyltrimethylammonium bromide
 57-88-5, Cholesterol, properties 58-33-3, Promethazine
 hydrochloride 69-09-0, Chlorpromazine hydrochloride
 112-00-5, Dodecyltrimethylammonium chloride 112-02-7,
 Hexadecyltrimethylammonium chloride 113-52-0, Imipramine
 hydrochloride 126-92-1, Sodium octyl sulfate 142-87-0,
 Sodium decyl sulfate 143-19-1, Sodium oleate 145-41-5,
 Sodium dehydrocholate 145-42-6, Sodium taurocholate
 151-21-3, Sodium dodecyl sulfate, properties 302-95-4,
 Sodium deoxycholate 361-09-1, Sodium cholate 629-25-4,
 Sodium dodecanoate 751-94-0, Sodium fusidate 863-57-0,
 Sodium glycocholate 871-95-4, Dimethyldodecylphosphine
 oxide 1002-62-6, Sodium decanoate 1119-94-4;
 Dodecyltrimethylammonium bromide 1119-97-7,
 Tetradecyltrimethylammonium bromide 1180-95-6, Sodium
 taurodeoxycholate 1191-50-0, Sodium tetradecyl sulfate
 1643-20-5, Dimethyldodecylamine oxide 1943-11-9,
 Nonyltrimethylammonium bromide 2082-84-0,
 Decyltrimethylammonium bromide 2083-68-3,
 Octyltrimethylammonium bromide 2190-95-6,
 Dimethyldecylphosphine oxide 2281-11-0, Zwittergent 3-16
 2364-67-2, (-)-Palmitoylcarnitine 2386-53-0, Sodium
 dodecylsulfonate 2536-13-2, Dimethylnonylamine oxide
 2605-78-9, Dimethyloctylamine oxide 2605-79-0,
 Dimethyldecylamine oxide 2646-38-0, Sodium
 chenodeoxycholate 3476-42-4 4574-04-3,
 Tetradecyltrimethylammonium chloride 6009-98-9, Sodium
 taurochenodeoxycholate 6994-45-2 7305-25-1,
 2-(Hexylsulfinyl)ethanol 7305-26-2, 3-
 (Hexylsulfinyl)propanol 7305-27-3, 4-
 (Hexylsulfinyl)butanol 7305-29-5, 3-
 (Octylsulfinyl)propanol 7305-30-8, 2-
 (Octylsulfinyl)ethanol 7333-16-6, 4-(Octylsulfinyl)butanol
 9002-93-1, Triton X-100 9004-77-7, Polyethylene glycol
 monobutyl ether 9004-95-9, Brij 56 9004-98-2, Brij 96
 9005-00-9, Polyoxyethylene monooctadecyl ether 9005-64-5,
 Tween 20 10124-65-9, Potassium dodecanoate 11024-24-1,
 Digitonin 13232-68-3, Dimethyloctylphosphine oxide
 14933-08-5, Zwittergent 3-12 15163-36-7, Zwittergent 3-10
 15178-71-9, Dimethylundecylamine oxide 16409-34-0, Sodium
 glycodeoxycholate 16564-43-5, Sodium
 glycochenodeoxycholate 17364-16-8 18656-38-7
 25518-54-1, (-)-Lauroylcarnitine 25597-07-3,
 (-)-Tetradecanoylcarnitine 27252-75-1, Polyoxyethylene
 monooctyl ether 29836-26-8, Octylglucoside 31726-34-8,
 Polyoxyethylene monohexyl ether 53892-41-4 64000-90-4,
 Tetramethylammonium dodecanoate, properties 69227-93-6
 75345-50-5, Glycerol monododecyl ether 75621-03-3, CHAPS
 82473-24-3, CHAPSO 100031-70-7 136023-79-5
 169149-55-7, BisCHAPSO
 ROLE: PRP (Properties)
 (calcn. of partial sp. vols. of detergents and lipids)

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L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 82473-24-3 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-
 [[[3 α ,5 β ,7 α ,12 α)-3,7,12-trihydroxy-24-oxocholan-24-
 yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:

CN Cholane, 1-propanaminium deriv.

OTHER NAMES:

CN 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate

CN **CHAPSO**

FS STEREOSEARCH

DR 120893-60-9

MF C32 H58 N2 O8 S

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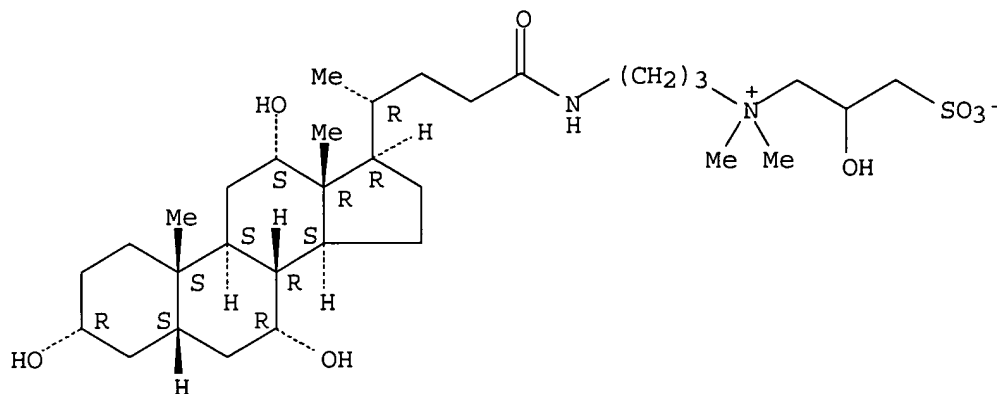
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|--------------------------|--------------------------|-------------------------|---------------------------|------------------------|----------------------|
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Absolute stereochemistry.



186 REFERENCES IN FILE CA (1907 TO DATE)

186 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 142:308767 CA
TITLE: Surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants
INVENTOR(S): Wang, Hui; Gai, Hongwei; Bai, Jiling; Lin, Bingcheng
PATENT ASSIGNEE(S): Dalian Research Institute of Chemicophysics, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
INT. PATENT CLASSIF.:
MAIN: G01N027-447

SECONDARY: G01N033-50; G01N033-543
 CLASSIFICATION: 80-2 (Organic Analytical Chemistry)
 Section cross-reference(s): 38, 79
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| CN 1469120 | A | 20040121 | CN 2002-132623 | 20020718 |
| PRIORITY APPLN. INFO.: | | | CN 2002-132623 | 20020718 |

ABSTRACT:

The microchannel surface treatment method of polymeric capillary electrophoresis chips is done by electrophoresis the chips in a phosphate buffer solution containing anionic, cationic, amphoteric or nonionic surfactants for electro dialysis current control. The anionic surfactant is sodium decylsulfate, sodium dodecylsulfate, sodium dodecylsulfonate, sodium tetradecylsulfate, polyoxyethylene dodecyl ether sodium sulfate, N-lauroyl-2-methylaminoethane-1-sulfonate, N-dodecyl-L-valine sodium salt, cholic acid, deoxycholic acid, taurocholic acid, and/or perfluoroheptanoic acid. The cationic surfactant is dodecyltrimethylammonium chloride, dodecyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, and/or cetyltrimethylammonium bromide. The amphoteric surfactant is cholamidopropyl dimethylaminopropanesulfonic acid and/or cholamidopropyl dimethylamino-2-hydroxypropanesulfonic acid. The nonionic surfactant is polyoxyethylene dodecyl ether, octyl glucoside, dodecyl- β -D-maltoside, and/or Triton X- 100.

SUPPL. TERM: PMMA capillary electrophoresis chip microchannel surface treatment; capillary electrophoresis device polymer; anionic cationic amphoteric nonionic surfactant surface treatment

INDEX TERM: Surfactants
 (amphoteric; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: Surfactants
 (anionic; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: Surfactants
 (cationic; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: Surfactants
 (nonionic; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: Capillary electrophoresis apparatus
 (polymer; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: 75621-03-3 82473-24-3
 ROLE: TEM (Technical or engineered material use); USES (Uses)
 (amphoteric surfactant; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: 81-24-3, Taurocholic acid 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 142-87-0, Sodium decylsulfate 151-21-3, Sodium dodecylsulfate, uses 375-85-9, Perfluoroheptanoic acid 1191-50-0 2386-53-0, Sodium dodecylsulfonate 3737-57-3 9004-82-4, Polyoxyethylene dodecyl ether sodium sulfate 37869-33-3, Sodium N-lauroylvaline
 ROLE: TEM (Technical or engineered material use); USES (Uses)
 (anionic surfactant; surface treatment of microchannels of polymeric capillary electrophoresis chips with surfactants)

INDEX TERM: 57-09-0, Cetyltrimethylammonium bromide 112-00-5,
Dodecyltrimethylammonium chloride 1119-94-4,
Dodecyltrimethylammonium bromide 1119-97-7,
Tetradecyltrimethylammonium bromide
ROLE: TEM (Technical or engineered material use); USES (Uses)
(cationic surfactant; surface treatment of microchannels
of polymeric capillary electrophoresis chips with
surfactants)

INDEX TERM: 9002-92-0, Brij 35 9002-93-1, Triton X-100 29836-26-8,
Octyl glucoside 69227-93-6, Dodecyl- β -D-maltoside
ROLE: TEM (Technical or engineered material use); USES (Uses)
(nonionic surfactant; surface treatment of microchannels
of polymeric capillary electrophoresis chips with
surfactants)

INDEX TERM: 9011-14-7, Polymethyl methacrylate
ROLE: POF (Polymer in formulation); TEM (Technical or
engineered material use); USES (Uses)
(surface treatment of microchannels of polymeric
capillary electrophoresis chips with surfactants)

REFERENCE 2

ACCESSION NUMBER: 142:217428 CA
TITLE: Conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551
AUTHOR(S): Ando, Akinori; Ogawa, Jun; Kishino, Shigenobu;
Shimizu, Sakayu
CORPORATE SOURCE: Division of Applied Life Sciences, Graduate School of
Agriculture, Kyoto University, Sakyo-ku, Kyoto,
606-8502, Japan
SOURCE: Enzyme and Microbial Technology (2004), 35(1), 40-45
CODEN: EMTED2; ISSN: 0141-0229
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 7

ABSTRACT:

The conditions for conjugated linoleic acid (CLA) production from castor oil, in which the main fatty acid component is ricinoleic acid, were investigated using washed cells of Lactobacillus plantarum JCM 1551 as the catalyst. In the presence of lipase, castor oil became an effective substrate for CLA production by the bacterium. Lipase M "Amano" 10 supported CLA production most effectively among the lipases tested. The addition of a detergent, especially Lubrol PX, enhanced the CLA production. The CLA produced comprised a mixture of two isomers, i.e. cis-9,trans-11-octadecadienoic acid (CLA1) and trans-9,trans-11-octadecadienoic acid (CLA2). Under the optimum conditions (1.0 M sodium citrate buffer, pH 6.0, 37°C) with castor oil as the substrate and washed cells of L. plantarum (12%, wet cell w/v) as the catalyst, 2.7 mg/mL CLA was produced from 5.0 mg/mL castor oil in 99 h (productivity, 0.027 mg/mL/h), and 7.5 mg/mL CLA from 30 mg/mL castor oil in 171 h (productivity, 0.044 mg/mL/h). In the former case, the CLA produced accounted for 45.5% of the total fatty acids obtained, and consisted of CLA1 (26%) and CLA2 (74%).

SUPPL. TERM: Lactobacillus castor oil conjugated linoleic acid
INDEX TERM: pH
(biol. effects of; conjugated linoleic acid production from
castor oil by Lactobacillus plantarum JCM 1551)

INDEX TERM: Enzymes, uses
ROLE: BCP (Biochemical process); CAT (Catalyst use); BIOL
(Biological study); PROC (Process); USES (Uses)
(com.; conjugated linoleic acid production from castor oil by

INDEX TERM: Lactobacillus plantarum JCM 1551)
Detergents
Lactobacillus plantarum
Temperature effects, biological
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

INDEX TERM: Castor oil
ROLE: BCP (Biochemical process); BIOL (Biological study); PROC
(Process)
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

INDEX TERM: Hydrolysis
(enzymic; conjugated linoleic acid production from castor oil
by Lactobacillus plantarum JCM 1551)

INDEX TERM: Albumins, processes
ROLE: BCP (Biochemical process); BIOL (Biological study); PROC
(Process)
(serum, bovine; conjugated linoleic acid production from
castor oil by Lactobacillus plantarum JCM 1551)

INDEX TERM: 60-33-3, Linoleic acid, processes 141-22-0, Ricinoleic
acid 302-95-4, Sodium deoxycholate 557-04-0, SM 1000
683-10-3 6004-24-6, N-Hexadecylpyridinium chloride
monohydrate 9002-92-0, Lubrol PX 9002-93-1, Triton x-305
9005-64-5, Tween 20 9005-65-6, Tween 80 9016-45-9,
Triton N101 9036-19-5, Nonidet p_40 25301-02-4, Triton
wr-1339 60864-33-7, Triton Cf-10 69227-93-6,
N-Dodecyl- β -D-maltoside 75621-03-3, CHAPS
82473-24-3, CHAPSO 85618-20-8 86303-22-2, BIGCHAP
86303-23-3, Deoxy_BIGCHAP
ROLE: BCP (Biochemical process); BIOL (Biological study); PROC
(Process)
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

INDEX TERM: 9001-62-1, Lipase M Amano 10
ROLE: BCP (Biochemical process); CAT (Catalyst use); BIOL
(Biological study); PROC (Process); USES (Uses)
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

INDEX TERM: 544-71-8P, trans-9,trans-11-Octadecadienoic acid
2540-56-9P, cis-9,trans-11-Octadecadienoic acid
ROLE: BMF (Bioindustrial manufacture); BIOL (Biological study);
PREP (Preparation)
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

INDEX TERM: 34932-12-2P
ROLE: BYP (Byproduct); PREP (Preparation)
(conjugated linoleic acid production from castor oil by
Lactobacillus plantarum JCM 1551)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

REFERENCE(S): (1) Ando, A; J Am Oil Chem Soc 2003, V80, P889 CAPLUS
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CAPLUS
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CAPLUS
(9) Kishino, S; Biosci Biotechnol Biochem 2003, V67, P179
CAPLUS
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REFERENCE 3

ACCESSION NUMBER: 142:110116 CA
 TITLE: Methods and kits for obtaining nucleic acid from biological samples
 INVENTOR(S): Montesclaros, Luz; Greenfield, I. Lawrence
 PATENT ASSIGNEE(S): Applera Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 29 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C12Q001-68
 SECONDARY: C12N001-08
 US PATENT CLASSIF.: 435006000
 CLASSIFICATION: 9-16 (Biochemical Methods)
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005009036 | A1 | 20050113 | US 2003-618493 | 20030711 |
| WO 2005007895 | A1 | 20050127 | WO 2004-US22250 | 20040709 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-618493 20030711

ABSTRACT:

Methods and kits for isolating nucleic acids from a sample, typically a biol. sample are disclosed. In certain embodiments, the methods and kits of the invention comprise at least one protease and at least one solid phase. In certain embodiments, the methods and kits of the invention comprise at least one chaotrope and at least one solid phase. In certain embodiments, the inventive methods and kits further comprise at least one chaotrope, at least one zwitterionic compound, at least one cationic detergent, at least one non-ionic detergent, or combinations thereof.

SUPPL. TERM: kit nucleic acid biol
 INDEX TERM: Named reagents and solutions
 Named reagents and solutions
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (CPD; methods and kits for obtaining nucleic acid from biol. samples)
 INDEX TERM: Betaines
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (C12-14-alkyldimethyl; methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: Detergents
(cationic; methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: Animal tissue culture
Anticoagulants
Bacillus licheniformis
Blood analysis
Human
Test kits
Zwitterions
(methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: DNA
Nucleic acids
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: Detergents
(nonionic; methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: 9014-01-1, Subtilisin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(Carlsberg; methods and kits for obtaining nucleic acid from biol. samples)

INDEX TERM: 50-01-1, Guanidine hydrochloride 57-09-0,
Cetyltrimethylammonium bromide 57-13-6, Urea, biological studies 60-00-4, EDTA, biological studies 62-56-6,
Thiourea, biological studies 112-00-5,
Dodecyltrimethylammonium chloride 112-02-7,
Cetyltrimethylammonium chloride 311-28-4,
Tetrabutylammonium iodide 333-20-0, Potassium thiocyanate 540-72-7, Sodium thiocyanate 593-84-0, Guanidinium thiocyanate 631-40-3, Tetrapropylammonium iodide 1112-67-0, Tetrabutylammonium chloride 1119-94-4,
Dodecyltrimethylammonium bromide 1119-97-7,
Tetradecyltrimethylammonium bromide 1643-19-2,
Tetrabutylammonium bromide 1643-20-5, Lauryldimethylamine N-oxide 1941-30-6, Tetrapropylammonium bromide 2082-84-0, Decyltrimethylammonium bromide 2281-11-0,
n-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 2644-64-6, Dipalmitoylphosphatidylcholine 4574-04-3,
Tetradecyltrimethylammonium chloride 5810-42-4,
Tetrapropylammonium chloride 7447-40-7, Potassium chloride, biological studies 7447-41-8, Lithium chloride, biological studies 7550-35-8, Lithium bromide 7601-89-0,
Sodium perchlorate 7631-86-9, Silica, biological studies 7647-15-6, Sodium bromide, biological studies 7681-11-0,
Potassium iodide, biological studies 7681-82-5, Sodium iodide, biological studies 7758-02-3, Potassium bromide, biological studies 9001-72-3, Pancreatic protease 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9005-49-6,
Heparin, biological studies 9036-06-0, Pronase 9073-78-3, Thermolysin 10377-51-2, Lithium iodide 13177-41-8, n-Octadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 14933-08-5, n-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 14933-09-6,
n-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 15163-30-1, N-Dodecyl-N,N-(dimethylammonio) butyrate 15163-36-7, n-Decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 15178-76-4, n-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate 15471-17-7 15510-55-1,

Dodecyltriphenylphosphonium bromide 28608-79-9,
Dodecylbetaine 29557-51-5, N-Dodecylphosphocholine
37259-58-8, Proteinase T 38880-58-9 39450-01-6
42613-33-2, Dispace 53255-89-3 58066-85-6,
N-Hexadecylphosphocholine 68207-00-1,
Dodecylethyldimethylammonium bromide 69772-87-8,
Thermitase 70504-28-8 75621-03-3, 3-[(3-
Cholamidopropyl)dimethylammonio]-1-propanesulfonate
77733-28-9 81239-45-4 82473-24-3, 3-[(3-
Cholamidopropyl)dimethylammonio]-2-hydroxy-1-
propanesulfonate 86303-22-2, BigCHAP 104702-33-2
120139-52-8 121150-44-5 129274-39-1 160255-06-1
160788-56-7 193695-21-5 253678-64-7 557788-85-9
675126-15-5 823796-65-2 823796-66-3
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(methods and kits for obtaining nucleic acid from biol.
samples)

REFERENCE 4

ACCESSION NUMBER: 141:420080 CA
TITLE: Amantadine partition and localization in phospholipid
membrane: a solution NMR study
AUTHOR(S): Wang, Junfeng; Schnell, Jason R.; Chou, James J.
CORPORATE SOURCE: Department of Biological Chemistry and Molecular
Pharmacology, Harvard Medical School, Boston, MA,
02115, USA
SOURCE: Biochemical and Biophysical Research Communications
(2004), 324(1), 212-217
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-5 (Pharmacology)
Section cross-reference(s): 9

ABSTRACT:

Quantification of membrane partition potential of drug compds. is of great pharmaceutical interest. Here, a novel approach combining liquid-state NMR diffusion measurements and fast-tumbling lipid/detergent bicelles is used to measure accurately the partition coefficient K_p of amantadine in phospholipid bilayers. Amantadine is found to have a strong membrane partition potential, with K_p of 27.6 in DMPC and 37.8 in POPC lipids. Electrostatic interaction also plays a major role in the drug's affinity towards biol. membrane as introduction of neg. charged POPG dramatically increases its K_p . Saturation transfer difference expts. in small bicelles indicate that amantadine localizes near the neg. charged phosphate group and the hydrocarbon chain of bilayer lipid. The approach undertaken in this study is generally applicable for characterizing interactions between small mols. and phospholipid membranes.

SUPPL. TERM: amantadine phospholipid membrane partition lipid detergent
bicelle NMR
INDEX TERM: Influenza
(A; soln NMR anal. of amantadine partition and
localization in phospholipid membrane)
INDEX TERM: Membrane, biological
(bilayer; soln NMR anal. of amantadine partition and
localization in phospholipid membrane)
INDEX TERM: NMR spectroscopy
(liquid-state; soln NMR anal. of amantadine partition and
localization in phospholipid membrane)
INDEX TERM: Molecular association
(of amantadine and DMPC; soln NMR anal. of amantadine

partition and localization in phospholipid membrane)

INDEX TERM: Antiviral agents
Diffusion
Electrostatic force
Influenza A virus
Partition
(soln NMR anal. of amantadine partition and localization in phospholipid membrane)

INDEX TERM: Phospholipids, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(soln NMR anal. of amantadine partition and localization in phospholipid membrane)

INDEX TERM: 768-94-5, Amantadine 18194-24-6, 1,2-Dimyristoyl-sn-glycero-3-phosphocholine 26853-31-6, Popc 34506-67-7, 1,2-Dicaproyl-sn-glycero-3-phosphocholine 82473-24-3, CHAPSO 185435-28-3, POPG
ROLE: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(soln NMR anal. of amantadine partition and localization in phospholipid membrane)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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REFERENCE 5

ACCESSION NUMBER: 141:310226 CA
TITLE: Papanicolau staining process
INVENTOR(S): Lapen, Daniel; Soule, Norman; Lim, Somthouck
PATENT ASSIGNEE(S): Cytoc Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: G01N001-30
 SECONDARY: G01N033-48
 US PATENT CLASSIF.: 435040500
 CLASSIFICATION: 9-4 (Biochemical Methods)
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004191854 | A1 | 20040930 | US 2003-404879 | 20030331 |
| WO 2004086945 | A2 | 20041014 | WO 2004-US9437 | 20040326 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-404879 20030331

ABSTRACT:

A method for treating a biol. sample with a Papanicolaou staining process is provided. The method comprises incorporating a detergent treatment into the staining process at any of various steps. The method has been found to advantageously reduce the number of artifacts produced during Papanicolaou staining. Also provided is a sample stained by such a process.

SUPPL. TERM: papanicolau staining process

INDEX TERM: Amines, biological studies

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (C12-14-alkyl, ethoxylated; papanicolau staining process)

INDEX TERM: Diagnosis

(agents; papanicolau staining process)

INDEX TERM: Detergents

(anionic; papanicolau staining process)

INDEX TERM: Analysis

Process automation

(automated anal.; papanicolau staining process)

INDEX TERM: Detergents

(cationic; papanicolau staining process)

INDEX TERM: Castor oil

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (ethoxylated; papanicolau staining process)

INDEX TERM: Human

Staining, biological

(papanicolau staining process)

INDEX TERM: Polyoxyalkylenes, biological studies

Saponins

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (papanicolau staining process)

INDEX TERM: Amines, biological studies

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (tallow alkyl, ethoxylated; papanicolau staining process)

INDEX TERM: 57-09-0, Hexadecyltrimethylammonium bromide 81-23-2,
 Dehydrocholic acid 81-25-4, Cholic acid 82-94-0, Light

Green 83-44-3, Deoxycholic acid 97-78-9,
 N-Lauroylsarcosine 112-92-5, 1-Octadecanol 122-18-9,
 Benzyltrimethylhexadecylammonium chloride 123-46-6
 124-03-8, Ethylhexadecyldimethylammonium bromide 126-92-1,
 Sodium octyl sulfate 128-13-2, Ursodeoxycholic acid
 139-08-2, Benzyltrimethyltetradecylammonium chloride
 139-88-8, Niaproof 4 143-62-4, Digitoxigenin 145-42-6,
 Sodium taurocholate 151-21-3, Sodium dodecyl sulfate,
 biological studies 302-95-4, Sodium deoxycholate
 360-65-6, Glycodeoxycholic acid 361-09-1, Sodium cholate
 474-25-9, Chenodeoxycholic acid 474-74-8, Glycolithocholic
 acid 475-31-0, Glycocholic acid 516-90-5,
 Tauroolithocholic acid 517-28-2, Hematoxylin 553-08-2,
 Thonzonium bromide 577-11-7, Triton GR-5 1119-94-4,
 Dodecyltrimethylammonium bromide 1119-97-7,
 Trimethyl(tetradecyl)ammonium bromide 1338-39-2, Span 20
 1338-41-6, Span 60 1338-43-8, Span 80 1643-20-5,
 N,N-Dimethyldodecylamine N-oxide 2044-56-6, Lithium
 dodecyl sulfate 2281-11-0 2420-29-3, Hexaethylene glycol
 monooctadecyl ether 3055-94-5, Triethylene glycol
 monododecyl ether 3055-95-6, Pentaethylene glycol
 monododecyl ether 3055-96-7, Hexaethylene glycol
 monododecyl ether 3055-98-9, Octaethylene glycol
 monododecyl ether 3055-99-0, Nonaethylene glycol
 monododecyl ether 3700-67-2, Dimethyldioctadecylammonium
 bromide 3944-72-7, 1-Octanesulfonic acid 4478-97-1,
 Pentaethylene glycol monohexadecyl ether 4484-59-7,
 Triethylene glycol monohexadecyl ether 4669-23-2,
 Triethylene glycol monodecyl ether 5157-04-0, Hexaethylene
 glycol monotetradecyl ether 5168-91-2, Hexaethylene glycol
 monohexadecyl ether 5274-68-0, Tetraethylene glycol
 monododecyl ether 5698-39-5, Octaethylene glycol
 monohexadecyl ether 5703-94-6, Tetraethylene glycol
 monodecyl ether 6009-98-9, Sodium taurochenodeoxycholate
 7281-04-1, Benzyltrimethylammonium bromide
 9002-92-0, Brij 30 9002-93-1, Triton X-100 9003-11-6
 9004-95-9, Brij 52 9004-98-2, Brij 97 9004-99-3,
 Polyoxyethylene stearate 9005-00-9, Brij 78 9005-64-5,
 TWEEN 21 9005-65-6, TWEEN 80 9005-66-7, TWEEN 40
 9005-67-8, TWEEN 61 9005-70-3, TWEEN 85 9005-71-4, TWEEN
 65 9014-93-1, Triton X-207 9016-45-9, Triton N
 9036-19-5, Igepal CA-520 9043-30-5 11024-24-1, Digitonin
 11105-10-5, Triton QS 15 12298-68-9, Potassium iodide
 (K(I3)) 12777-77-4, Fast Green 13149-87-6 13177-41-8
 14605-22-2, Tauroursodeoxycholic acid 14933-08-5,
 3-(Dodecyltrimethyl ammonio)propanesulfonate 14933-09-6
 15163-36-7 15178-76-4 16023-35-1, 1-Propanesulfonic acid
 ion (-1) 16564-43-5, Sodium glycochenodeoxycholate
 17372-87-1, Eosin Y 18449-82-6, Tetradecyl- β -D-
 maltoside 19327-38-9, Triethylene glycol monooctyl ether
 19327-40-3, Pentaethylene glycol monooctyl ether
 23244-49-7, Pentaethylene glycol monodecyl ether
 24233-81-6, Octaethylene glycol monodecyl ether
 24613-77-2, 1-Butanesulfonate 24613-78-3, Hexanesulfonate
 24708-25-6, Pentanesulfonate 24708-26-7, 1-Heptanesulfonic
 acid ion(-1) 24938-91-8, Polyoxyethylene tridecyl ether
 25301-02-4, Tyloxapol 25322-68-3D, Polyethylene glycol,
 derivs. 26266-57-9, Span 40 26266-58-0, Span 85
 26403-72-5, Polyethylene glycol diglycidyl ether
 26658-19-5, Span 65 26826-30-2, Triethylene glycol
 monotetradecyl ether 27847-86-5, Octaethylene glycol
 monotetradecyl ether 29781-81-5, n-Decyl
 α -D-glucopyranoside 29836-26-8, Octyl- β -D-

glucopyranoside 37211-53-3, Triton CF 21 37211-54-4,
Triton CF 32 37281-47-3, Triton DF-12 38411-85-7, Sodium
taurohyodeoxycholate 38480-64-7, 1-Dodecanesulfonic acid,
ion(-1) 39034-24-7, Tetraethylene glycol monotetradecyl
ether 39840-09-0, Heptaethylene glycol monododecyl ether
40036-79-1, Heptaethylene glycol monotetradecyl ether
45102-30-5, 1-Nonanesulfonic acid ion (-1) 45131-92-8,
1-Decanesulfonate 50996-85-5 52623-95-7, Triton QS-44
55348-40-8, Triton X-200 58229-81-5, Triton DF-16
59122-55-3 59979-06-5, Triton X-151 68207-00-1,
Dodecylethyldimethylammonium bromide 69227-93-6, n-Dodecyl
 β -D-maltoside 69364-63-2, Polyoxyethylene
isohexadecyl ether 70005-86-6, Undecyl
 β -D-glucopyranoside 70699-07-9 71093-13-5,
Pentaethylene glycol monooctadecyl ether 75621-03-3, CHAPS
75718-57-9, Niaproof 82473-24-3, CHAPSO 82494-09-5,
Decyl β -D-maltopyranoside 85182-91-8,
2-Bromoethanesulfonate 85261-19-4 85261-20-7, MEGA 10
85316-98-9, MEGA 8 86303-22-2, BigCHAP 86674-95-5,
Pentaethylene glycol monohexyl ether 87246-72-8
98060-40-3 98064-96-1 115457-83-5 116183-64-3, Dodecyl
 α -D-maltoside 121309-88-4, Benzyltrimethylammonium
tetrachloroiodate
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(papanicolau staining process)

REFERENCE 6

ACCESSION NUMBER: 141:238713 CA
TITLE: Purification and Characterization of the Human
 γ -Secretase Complex
AUTHOR(S): Fraering, Patrick C.; Ye, Wenjuan; Strub, Jean-Marc;
Dolios, Georgia; LaVoie, Matthew J.; Ostaszewski, Beth
L.; van Dorsselaer, Alain; Wang, Rong; Selkoe, Dennis
J.; Wolfe, Michael S.
CORPORATE SOURCE: Center for Neurologic Diseases, Brigham and Women's
Hospital and Harvard Medical School, Boston, MA,
02115, USA
SOURCE: Biochemistry (2004), 43(30), 9774-9789
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 7-3 (Enzymes)
Section cross-reference(s): 6, 13

ABSTRACT:

γ -Secretase is a member of an unusual class of proteases with
intramembrane catalytic sites. This enzyme cleaves many type I membrane
proteins, including the amyloid β -protein (A β) precursor (APP) and
the Notch receptor. Biochem. and genetic studies have identified four membrane
proteins as components of γ -secretase: heterodimeric presenilin (PS)
composed of its N- and C-terminal fragments (PS-NTF/CTF), a mature glycosylated
form of nicastrin (NCT), Aph-1, and Pen-2. Recent data from studies in
Drosophila, mammalian, and yeast cells suggest that PS, NCT, Aph-1, and Pen-2
are necessary and sufficient to reconstitute γ -secretase activity.
However, many unresolved issues, in particular the possibility of other
structural or regulatory components, would be resolved by actually purifying
the enzyme. Here, we report a detailed, multistep purification procedure for active
 γ -secretase and an initial characterization of the purified protease.
Extensive mass spectrometry of the purified proteins strongly suggests that
PS-NTF/CTF, mNCT, Aph-1, and Pen-2 are the components of active
 γ -secretase. Using the purified γ -secretase, we describe factors

that modulate the production of specific A β species: (1) phosphatidylcholine and sphingomyelin dramatically improve activity without changing cleavage specificity within an APP substrate; (2) increasing CHAPSO concns. from 0.1 to 0.25% yields a .apprx.100% increase in A β 42 production; (3) exposure of an APP-based recombinant substrate to 0.5% SDS modulates cleavage specificity from a disease-mimicking pattern (high A β 42/43) to a physiol. pattern (high A β 40); and (4) sulindac sulfide directly and preferentially decreases A β 42 cleavage within the purified complex. Taken together, our results define a procedure for purifying active γ -secretase and suggest that the lipid-mediated conformation of both enzyme and substrate regulate the production of the potentially neurotoxic A β 42 and A β 43 peptides.

SUPPL. TERM: gamma secretase human nicastrin presenilin Aph1 Pen2;
amyloid beta protein precursor

INDEX TERM: Enzyme functional sites
(active; γ -secretase is composed of presenilin,
glycosylated form of nicastrin, Aph-1 and Pen-2 membrane
proteins)

INDEX TERM: Human
(lipid-mediated conformation of both γ -secretase
and amyloid β -protein precursor regulate production of
potentially neurotoxic amyloid β -protein precursor
peptides)

INDEX TERM: Amyloid precursor proteins
Phosphatidylcholines, biological studies
Sphingomyelins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(lipid-mediated conformation of both γ -secretase
and amyloid β -protein precursor regulate production of
potentially neurotoxic amyloid β -protein precursor
peptides)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(membrane, Aph-1; γ -secretase is composed of
presenilin, glycosylated form of nicastrin, Aph-1 and
Pen-2 membrane proteins)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(membrane, Pen-2; γ -secretase is composed of
presenilin, glycosylated form of nicastrin, Aph-1 and
Pen-2 membrane proteins)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(nicastrin; γ -secretase is composed of presenilin,
glycosylated form of nicastrin, Aph-1 and Pen-2 membrane
proteins)

INDEX TERM: Conformation
(protein; CHAPSO and sodium dodecyl sulfate promotes
amyloid β -protein precursor cleavage)

INDEX TERM: Protein motifs
(transmembrane domain; CHAPSO and sodium dodecyl sulfate
promotes amyloid β -protein precursor transmembrane
domain cleavage)

INDEX TERM: Presenilins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(γ -secretase is composed of presenilin,
glycosylated form of nicastrin, Aph-1 and Pen-2 membrane
proteins)

INDEX TERM: 151-21-3, Sodium dodecyl sulphate, biological studies
82473-24-3, CHAPSO
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CHAPSO and sodium dodecyl sulfate promotes amyloid β -protein precursor cleavage)

INDEX TERM: 749376-90-7 749376-91-8
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid-mediated conformation of both γ -secretase and amyloid β -protein precursor regulate production of potentially neurotoxic amyloid β -protein precursor peptides)

INDEX TERM: 338454-52-7, γ -Secretase
ROLE: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(γ -secretase is composed of presenilin, glycosylated form of nicastrin, Aph-1 and Pen-2 membrane proteins)

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REFERENCE 7

ACCESSION NUMBER: 141:152866 CA
 TITLE: Effect of Membrane Perturbants on the Activity and Phase Distribution of Inositol Phosphorylceramide Synthase; Development of a Novel Assay
 AUTHOR(S): Aeed, Paul A.; Sperry, Andrea E.; Young, Casey L.; Nagiec, Marek M.; Elhammer, Ake P.
 CORPORATE SOURCE: Pharmacia Corporation, Kalamazoo, MI, 49001, USA
 SOURCE: Biochemistry (2004), 43(26), 8483-8493
 CODEN: BICHAW; ISSN: 0006-2960
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 CLASSIFICATION: 7-1 (Enzymes)

ABSTRACT:
 The effect of 26 different membrane-perturbing agents on the activity and phase distribution of inositol phosphorylceramide synthase (IPC synthase) activity in crude *Candida albicans* membranes was investigated. The nonionic detergents Triton X-100, Nonidet P-40, Brij, Tween, and octylglucoside all inactivated the enzyme. However, at moderate concns., the activity of the Triton X-100- and octylglucoside-solubilized material could be partially restored by inclusion of 5 mM phosphatidylinositol (PI) in the solubilization buffer. The apparent mol.

mass of IPC synthase activity solubilized in 2% Triton X-100 was between 1.5 + 106 and 20 + 106 Da, while under identical conditions, octylglucoside-solubilized activity remained associated with large presumably membrane-like structures. Increased detergent concns. produced more drastic losses of enzymic activity. The zwitterionic detergents Empigen BB, N-dodecyl-N,N-(dimethylammonio)butyrate (DDMAB), Zwittergent 3-10, and amidosulfobetaine (ASB)-16 all appeared capable of solubilizing IPC synthase. However, these agents also inactivated the enzyme essentially irreversibly. Solubilization with lysophospholipids again resulted in drastic losses of enzymic activity that were not restored by the inclusion of PI. Lysophosphatidylinositol also appeared to compete, to some extent, with the donor substrate phosphatidylinositol. The sterol-containing agent digitonin completely inactivated IPC synthase. By contrast, sterol-based detergents such as 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), and taurodeoxycholate (tDOC) had little or no effect on the enzyme activity. The IPC synthase activity in *C. Albicans* membranes remained largely intact and sedimentable at CHAPS concns. (4%) where >90% of the phospholipids and 60% of the total proteins were extracted from the membranes. At 2.5% CHAPS, a concentration

where .apprx.50% of the protein and 80% of the phospholipids are solubilized, there was no detectable loss of enzyme activity, and the detergent-treated membranes had significantly improved properties compared to crude, untreated membranes as the source of IPC synthase activity. In contrast to assays utilizing intact membranes or Triton X-100 exts., assays using CHAPS- or tDOC-washed membranes were found to be reproducible, completely dependent on added acceptor substrate (C6-7-nitro-2-1,3-benzoxadiazol-4-yl (NBD)-ceramide), and >95% dependent on added donor substrate (PI). Product formation was linear with respect to both enzyme concentration and time, and transfer efficiency was improved more than 20-fold as compared to assays using crude membranes.

Determination

of kinetic parameters for the two IPC synthase substrates using CHAPS-washed membranes resulted in Km values of 3.3 and 138.0 μ M for C6-NBD-ceramide and PI, resp. In addition, the donor substrate, PI, was found to be inhibitory at high concns. with an apparent Ki of 588.2 μ M.

SUPPL. TERM: inositol phosphorylceramide synthase membrane perturbant phase
INDEX TERM: Betaines
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(C12-14-alkyldimethyl, membrane perturbant; membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)
INDEX TERM: Lysophosphatides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(lysophosphatidylglycerols, membrane perturbant; membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)
INDEX TERM: Lysophosphatidylcholines
Lysophosphatidylethanolamines
Lysophosphatidylinositols
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(membrane perturbant; membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)
INDEX TERM: *Candida albicans*
Enzyme kinetics
Membrane, biological

Membrane phases, biological

Solubilization

(membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)

INDEX TERM: 112-80-1, Oleic acid, biological studies 151-21-3, SDS, biological studies 516-50-7 9002-92-0, Brij 35 9002-93-1, Triton X-100 9004-95-9, Brij 58 9005-64-5, Tween 20 9005-65-6, Tween 80 9016-45-9, Triton N-60 9036-19-5, Nonidet P-40 11024-24-1, Digitonin 15163-30-1, DDMAB 15163-36-7, Zwittergent 3-10 29836-26-8, Octylglucoside 52562-29-5, ASB 16 69227-93-6 75621-03-3, CHAPS 82473-24-3, CHAPSO 85618-21-9 148565-56-4 228579-27-9

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

• (membrane perturbant; membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)

INDEX TERM: 157482-45-6, Inositol phosphorylceramide synthase

ROLE: ANT (Analyte); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(membrane perturbants effects on activity and phase distribution of inositol phosphorylceramide synthase in relation to enzyme assay)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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REFERENCE 8

ACCESSION NUMBER: 141:119301 CA
 TITLE: Improving the accuracy of luciferase-based assays for
 high throughput screening by using tolerance
 enhancement agents
 INVENTOR(S): Hawkins, Erika; Cali, James J.; Ho, Samuel Kin Sang;
 O'Brien, Martha; Somberg, Richard; Bulleit, Robert F.;
 Wood, Keith V.
 PATENT ASSIGNEE(S): Promega Corporation, USA
 SOURCE: PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: G01N
 CLASSIFICATION: 7-1 (Enzymes)
 Section cross-reference(s): 9
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2004059294 | A2 | 20040715 | WO 2003-US41454 | 20031223 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005026171 | A1 | 20050203 | US 2003-746995 | 20031223 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2002-436173P | 20021223 |
| | | | US 2003-444264P | 20030131 |
| | | | US 2003-447334P | 20030213 |

ABSTRACT:

The invention concerns methods and kits for improving the accuracy of luciferase-based assays for high throughput screening of compound libraries by reducing the number of false hits. A method and kit is provided for enhancing the tolerance of an assay reagent to compds. in an assay sample, the assay reagent

including a luciferase enzyme. The method includes contacting the luciferase with a tolerance enhancement agent in an amount sufficient to substantially protect luciferase enzyme activity from interference of the compound and minimize interference by at least about 10% relative to an assay not having tolerance enhancement agent. Tolerance-enhancing effect of detergents on the inhibition of luciferase was studied. Minimization of false hit occurrence using tolerance enhancement agents such as detergents was demonstrated.

SUPPL. TERM: luciferase assay tolerance enhancement agent detergent false hit screening

INDEX TERM: Surfactants
(anionic, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Surfactants
(cationic, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Castor oil
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)

(ethoxylated, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: High throughput screening
Luminescence, bioluminescence
Luminescence spectroscopy
Test kits
(improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Polyoxyalkylenes, analysis
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
(improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Enzymes, biological studies
ROLE: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(non-luminogenic; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Surfactants
(nonionic, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Amino acids, uses
Peptides, uses
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reaction products, with aminoluciferin; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Surfactants
(tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Crown ethers
Polyoxyalkylenes, analysis
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
(tolerance enhancement agent; improving accuracy of

luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: Surfactants
(zwitterionic, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 9016-45-9, Triton N101
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
(Tergitol NP 9, tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 9001-92-7, Protease
ROLE: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Trypsinase; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 9002-07-7, Trypsin 9013-05-2, Phosphatase 9031-44-1, Kinase 9035-51-2, Cytochrome P450, biological studies 169592-56-7, Caspase-3 179241-78-2, Caspase-8 180189-96-2, Caspase-9 186322-81-6, Caspase 189258-14-8, Caspase-7 372092-80-3, Protein kinase
ROLE: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 56-65-5, 5'-ATP, uses 58-64-0, 5'-ADP, uses 9014-00-0, Luciferase 61869-41-8, Renilla luciferase 61970-00-1, Firefly luciferase
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 2591-17-5D, D-Luciferin, derivs. 5571-98-2D, reaction products with amino acids or peptides
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(luminogenic substrate; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 57-09-0, CTAB 83-44-3 9002-92-0, Brij 35 9002-93-1, Triton X-100 9003-39-8, Polyvinyl pyrrolidone 9003-47-8, Polyvinyl pyridine 9004-95-9, Brij 58 9014-85-1 10016-20-3, α -Cyclodextrin 12619-70-4, Cyclodextrin 25322-68-3, PEG 75621-03-3, Chaps 82473-24-3, Chapso 86303-22-2, Bigchap 106392-12-5, Pluronic L64 188309-93-5, Chemal LA-9 722509-19-5, Pierce C 08 722509-82-2, Pierce C 10
ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
(tolerance enhancement agent; improving accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 723025-70-5 723025-71-6 723025-72-7 723025-73-8
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; improving the accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

INDEX TERM: 723025-66-9 723025-67-0 723025-68-1 723025-69-2
ROLE: PRP (Properties)

(unclaimed protein sequence; improving the accuracy of luciferase-based assays for high throughput screening by using tolerance enhancement agents)

REFERENCE 9

ACCESSION NUMBER: 141:50129 CA
TITLE: Assay for gamma secretase modulators
INVENTOR(S): Beher, Dirk
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: Brit. UK Pat. Appl., 30 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
 MAIN: C12Q001-37
 SECONDARY: C12N009-64
CLASSIFICATION: 9-2 (Biochemical Methods)
Section cross-reference(s): 7, 14
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| GB 2396415 | A1 | 20040623 | GB 2003-28875 | 20031212 |
| US 2004132114 | A1 | 20040708 | US 2003-739485 | 20031218 |
| PRIORITY APPLN. INFO.: | | | GB 2002-29582 | 20021219 |

ABSTRACT:

An assay for identifying compds. that interact with the γ -secretase complex comprising preparing and solubilizing a source of the complex, incubating a test compound together with an affinity probe and the source, capturing the resulting bound complex, and analyzing the components of the complex to determine whether the test compound has interacted with the complex by determining the amount of PS1-NTF, PS1-CTF or mature nicastrin present in the complex. The assay may be used in the identification of components of the γ -secretase complex.

SUPPL. TERM: assay gamma secretase
INDEX TERM: Presenilins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (1; assay for gamma secretase modulators)
INDEX TERM: Proteins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (PEN-2, APH-1; assay for gamma secretase modulators)
INDEX TERM: Alzheimer's disease
 (assay for gamma secretase modulators)
INDEX TERM: Nerve, neoplasm
 (neuroblastoma; assay for gamma secretase modulators)
INDEX TERM: Proteins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (nicastrin; assay for gamma secretase modulators)
INDEX TERM: 82473-24-3, CHAPSO
 ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
 (assay for gamma secretase modulators)
INDEX TERM: 392658-40-1
 ROLE: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
 (assay for gamma secretase modulators)

INDEX TERM: 338454-52-7, γ -Secretase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(assay for gamma secretase modulators)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD.

- (1) Anon; WO 2001075435 A3 CAPLUS
- (2) Anon; WO 2003008635 A3 CAPLUS
- (3) Beher; Biochemistry 2003, V42, P8133 CAPLUS
- (4) Kornilova; J Biol Chem 2003, V278, P16470 CAPLUS
- (5) Pinnix; J Biol Chem 2001, V276, P481 CAPLUS
- (6) Weihofen; J Biol Chem 2003, V278, P16528 CAPLUS

REFERENCE 10

ACCESSION NUMBER: 141:40332 CA
TITLE: Production of nano-carbon dissolving and purifying aqueous solutions
INVENTOR(S): Fuugetsu, Bunshi
PATENT ASSIGNEE(S): Hokkaido Technology Licensing Office Co., Ltd., Japan
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
INT. PATENT CLASSIF.:
MAIN: C01B031-02
CLASSIFICATION: 49-1 (Industrial Inorganic Chemicals)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2004052782 | A1 | 20040624 | WO 2002-JP12815 | 20021206 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| WO 2004060798 | A1 | 20040722 | WO 2003-JP15445 | 20031202 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.:

WO 2002-JP12815 20021206

ABSTRACT:

The alkaline dissolving solution contains phospholipid- or non-phospholipid surfactants forming 50-300 nm of microspore, nano-carbon permeable substance of Li+, and a persulfate as an oxidizing agent. The surfactant is selected from ≥ 1 of distearoyl phosphatidylcholine, dimyristoyl phosphatidylcholine, dipalmitoyl phosphatidylcholine, 3-[(3-colamidepropyl)dimethylamino]-2-hydroxy-1-propane sulfonate, 3-[(3-colamidepropyl)dimethylamino]-1-propane sulfonate, and N,N-bis(3-D-gluconamidopropyl)deoxycholamide. Nano-carbon containing raw

material is added into the solution for purification

SUPPL. TERM: nanocarbon dissoln purifn surfactant oxidizing agent
INDEX TERM: Nanotubes
(carbon; production of nano-carbon dissolving and purifying aqueous solns.)
INDEX TERM: Peroxysulfates
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(peroxydisulfates; production of nano-carbon dissolving and purifying aqueous solns.)
INDEX TERM: Surfactants
(phospholipid, non-phospholipid; production of nano-carbon dissolving and purifying aqueous solns.)
INDEX TERM: Oxidizing agents
(production of nano-carbon dissolving and purifying aqueous solns.)
INDEX TERM: 63-89-8, Dipalmitoyl phosphatidylcholine 816-94-4, Distearoyl phosphatidylcholine 18194-24-6, Dimyristoyl phosphatidylcholine 75621-03-3, 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate 82473-24-3, 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate 86303-23-3, N,N'-Bis(3-D-gluconamidopropyl)deoxycholamide
ROLE: MOA (Modifier or additive use); RGT (Reagent); RACT (Reactant or reagent); USES (Uses)
(production of nano-carbon dissolving and purifying aqueous solns.)

=>


```

=> s cholan
L8      16541 CHOLAN

=> s 18 and dimethylamino propyl
      464759 DIMETHYLAMINO
      2158470 PROPYL
      4 PROPYLS
      2158470 PROPYL
      (PROPYL OR PROPYLS)
      42929 DIMETHYLAMINO PROPYL
      (DIMETHYLAMINO(W) PROPYL)
L9      2 L8 AND DIMETHYLAMINO PROPYL

=> s 19 and 11
L10     0 L9 AND L1

=> d iall 19 1-2

L9      ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2005 ACS on STN
RN      204075-64-9  REGISTRY
ED      Entered STN:  14 Apr 1998
CN      Cholan-24-oic acid, 7,12-dihydroxy-3-[[6-[(1-oxo-2-
propenyl)amino]hexyl]oxy]-, monosodium salt, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12
 $\alpha$ )-, polymer with N-[3-(dimethylamino)propyl]-2-methyl-2-propenamide
hydrochloride (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN      2-Propenamide, N-[3-(dimethylamino)propyl]-2-methyl-, hydrochloride,
polymer with (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-7,12-dihydroxy-3-[[6-
[(1-oxo-2-propenyl)amino]hexyl]oxy]cholan-24-oic acid monosodium salt
(9CI)
FS      STEREOSEARCH
MF      (C33 H55 N O6 . C9 H18 N2 O . x Cl H . Na)x
CI      PMS
PCT     Polyacrylic, Polyester, Polyester formed
SR      CA
LC      STN Files:  CA, CAPLUS
DT.CA   Caplus document type:  Patent
RL.P    Roles from patents:  BIOL (Biological study); PREP (Preparation); USES
(Uses)

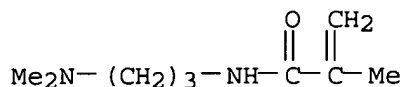
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Ring System Data

| Elemental Analysis EA | Elemental Sequence ES | Size of the Rings SZ | Ring System Formula RF | Ring Identifier RID | RID Occurrence Count |
|-----------------------------|-----------------------------|----------------------------|------------------------------|---------------------------|----------------------------|
| ===== | ===== | ===== | ===== | ===== | ===== |
| C5-C6-C6-C6 | C5-C6-C6-C6 | 5-6-6-6 | C17 | 4432.3.1 | 1 in CM 2 |

CM 1

CRN 204075-63-8 (5205-93-6)
CMF C9 H18 N2 O . x Cl H

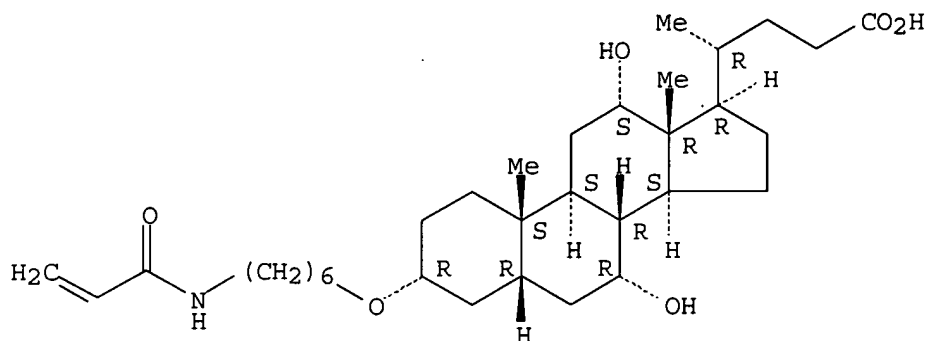


CM 2

CRN 204075-47-8 (212011-88-6)

CMF C33 H55 N O6 . Na

Absolute stereochemistry.



● Na

1 REFERENCES IN FILE CA (1907 TO DATE)

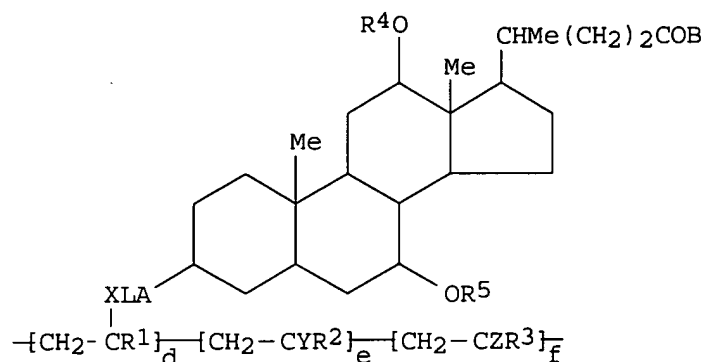
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 128:201062 CA
TITLE: Polymeric bile acid resorption inhibitors with simultaneous bile acid-adsorbing action
INVENTOR(S): Von Seggern, Heinke; Kramer, Werner; Wess, Guenther
PATENT ASSIGNEE(S): Hoechst Research & Technology Deutschland G.m.b.H. & Co. K.-G., Germany; Von Seggern, Heinke; Kramer, Werner; Wess, Guenther
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K047-48
CLASSIFICATION: 1-10 (Pharmacology)
Section cross-reference(s): 35
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------|
| WO 9807449 | A2 | 19980226 | WO 1997-EP4049 | 19970725 |
| WO 9807449 | A3 | 19980625 | | |
| W: CA, JP, MX, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19633268 | A1 | 19980226 | DE 1996-19633268 | 19960819 |
| CA 2263671 | AA | 19980226 | CA 1997-2263671 | 19970725 |
| EP 918544 | A2 | 19990602 | EP 1997-940028 | 19970725 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2000517356 | T2 | 20001226 | JP 1998-510319 | 19970725 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | DE 1996-19633268 | 19960819 |
| | | | WO 1997-EP4049 | 19970725 |

GRAPHIC IMAGE:



ABSTRACT:

Vinyl copolymers are disclosed which contain bile acid-adsorbing sites such as quaternary ammonium groups and are conjugated, directly or via a spacer, to a bile acid mol. or bile acid resorption inhibitor which binds to bile acid receptors. These polymers, of formula I [R1-R3 = H, CH3; R4, R5 = H, C1-6 alkyl or acyl; A = O, NH, bond; B = OH, ONa, OK, (substituted) amino; L = bond, NH, C(O), alkylene, Ar, N- or O-containing linker; Ar = arylene; X = bond, CH2, Ar, ArCH2; Y, Z = NH2, (substituted) amino or quaternary ammonium-containing group, CO2H, etc.; d = 0.01-1.00; e, f = 0-0.99; d + e + f = 1], cannot be resorbed owing to their high mol. weight, and prevent the accumulation of unresorbed bile acids in the intestine which could lead to diarrhea. I are suitable for treating lipid metabolism disturbances. Thus, cholic acid was converted to the 3-mesylate, then by substitution to the triethylene glycol ether, which was tosylated and conjugated to polyvinylamine with a degree of substitution of 1%. In an alternative procedure, Me 3-acryloylcholate was copolymd. with 3-methacrylamidopropyltrimethylammonium chloride using VA 044 as initiator, and the product was neutralized with NaOH. The addition product of Me 3-acryloylcholate to polyvinylamine adsorbed 52% of Na taurocholate and Na glycocholate from aqueous solution, compared to 33% for cholestyramine.

SUPPL. TERM: bile acid resorption inhibitor polymer conjugate; adsorption
bile acid vinyl polymer

INDEX TERM: Bile acids

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(conjugates, with polymers; polymeric bile acid
resorption inhibitors with simultaneous bile
acid-adsorbing action)

INDEX TERM: Circulation
(enterohepatic; polymeric bile acid resorption inhibitors
with simultaneous bile acid-adsorbing action)

INDEX TERM: Adsorption
Antiartherosclerotics
Anticholesteremic agents
Detergents
Digestive tract
Hypolipemic agents
Intestine
Resorption, animal
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

INDEX TERM: Bile acids

ROLE: BPR (Biological process); BSU (Biological study,

unclassified); BIOL (Biological study); PROC (Process)
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

INDEX TERM: Vinyl compounds, biological studies

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(polymers, conjugates with bile acid resorption
inhibitors; polymeric bile acid resorption inhibitors
with simultaneous bile acid-adsorbing action)

INDEX TERM: Lipids, biological studies

ROLE: BPR (Biological process); BSU (Biological study,
unclassified); BIOL (Biological study); PROC (Process)
(resorption of; polymeric bile acid resorption inhibitors
with simultaneous bile acid-adsorbing action)

INDEX TERM: Diet
(supplements; polymeric bile acid resorption inhibitors
with simultaneous bile acid-adsorbing action)

INDEX TERM: 81-25-4DP, Cholic acid, conjugates with polymers
26336-38-9DP, Polyvinylamine, conjugates with bile acids
204075-40-1P 204075-46-7P 204075-48-9P 204075-59-2P
204075-61-6P 204075-64-9P 204075-68-3P 204075-70-7DP,
saponified 204075-71-8DP, saponified 204075-92-3P
204075-95-6P 204075-98-9P 204076-00-6P 204076-02-8P
204076-03-9P

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

INDEX TERM: 81-24-3, Taurocholic acid 145-42-6, Sodium taurocholate
360-65-6, Glycodeoxycholic acid 475-31-0, Glycocholic acid
516-35-8, Taurochenodeoxycholic acid 516-50-7;
Taurodeoxycholic acid 640-79-9, Glycochenodeoxycholic acid
863-57-0, Sodium glycocholate

ROLE: BPR (Biological process); BSU (Biological study,
unclassified); BIOL (Biological study); PROC (Process)
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

INDEX TERM: 81-25-4, Cholic acid 100-02-7, p-Nitrophenol, reactions
109-85-3, 2-Methoxyethylamine 112-27-6 629-03-8,
1,6-Dibromohexane 4101-68-2, 1,10-Dibromodecane
5205-93-6 71550-12-4, Poly(allylamine hydrochloride)
204075-50-3

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

INDEX TERM: 72090-85-8P 135053-65-5P 204075-37-6P 204075-38-7P
204075-41-2P 204075-42-3P 204075-43-4P 204075-44-5P
204075-49-0P 204075-54-7P 204075-56-9P 204075-69-4P
204076-04-0P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(polymeric bile acid resorption inhibitors with
simultaneous bile acid-adsorbing action)

L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 76555-98-1 REGISTRY

ED Entered STN: 16 Nov 1984

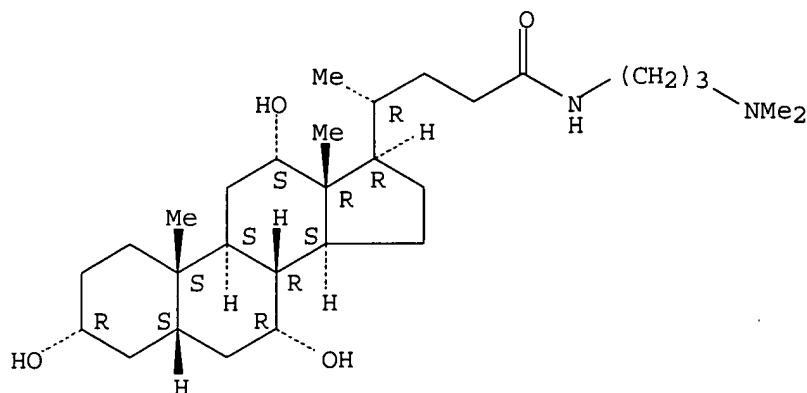
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

FS STEREOSEARCH
 MF C29 H52 N2 O4
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
 DT.CA Caplus document type: Journal; Patent
 RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 RLD.P Roles for non-specific derivatives from patents: USES (Uses)
 RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Ring System Data

| Elemental Analysis EA | Elemental Sequence ES | Size of the Rings SZ | Ring System Formula RF | Ring Identifier RID | RID Occurrence Count |
|-----------------------------|-----------------------------|----------------------------|------------------------------|---------------------------|----------------------------|
| ===== | ===== | ===== | ===== | ===== | ===== |
| C5-C6-C6-C6 | C5-C6-C6-C6 | 5-6-6-6 | C17 | 4432.3.1 | 1 |

Absolute stereochemistry.



Predicted Properties (PPROP)

| PROPERTY (CODE) | VALUE | CONDITION | NOTE |
|--------------------------|---------------------|------------|---------|
| Bioconc. Factor (BCF) | 1 | pH 1 | (1) ACD |
| Bioconc. Factor (BCF) | 1 | pH 4 | (1) ACD |
| Bioconc. Factor (BCF) | 1 | pH 7 | (1) ACD |
| Bioconc. Factor (BCF) | 1.00 | pH 8 | (1) ACD |
| Bioconc. Factor (BCF) | 22.4 | pH 10 | (1) ACD |
| Boiling Point (BP) | 658.6+/-55.0 deg C | 760.0 Torr | (1) ACD |
| Enthalpy of Vap. (HVPAP) | 110.99+/-6.0 kJ/mol | | (1) ACD |
| Flash Point (FP) | 352.1+/-56.7 deg C | | (1) ACD |
| H acceptors (HAC) | 6 | | (1) ACD |
| H donors (HD) | 4 | | (1) ACD |
| Koc (KOC) | 1 | pH 1 | (1) ACD |
| Koc (KOC) | 1 | pH 4 | (1) ACD |
| Koc (KOC) | 1.66 | pH 7 | (1) ACD |
| Koc (KOC) | 13.5 | pH 8 | (1) ACD |
| Koc (KOC) | 300 | pH 10 | (1) ACD |
| logD (LOGD) | -0.88 | pH 1 | (1) ACD |
| logD (LOGD) | -0.88 | pH 4 | (1) ACD |

| | | | |
|----------------------------|---------------------|------------|---------|
| logD (LOGD) | -0.14 | pH 7 | (1) ACD |
| logD (LOGD) | 0.77 | pH 8 | (1) ACD |
| logD (LOGD) | 2.11 | pH 10 | (1) ACD |
| logP (LOGP) | 2.221+/-0.427 | | (1) ACD |
| Molar Solubility (SLB.MOL) | >=0.01 - <0.1 mol/L | pH 1 | (1) ACD |
| Molar Solubility (SLB.MOL) | >=0.01 - <0.1 mol/L | pH 4 | (1) ACD |
| Molar Solubility (SLB.MOL) | <0.01 mol/L | pH 7 | (1) ACD |
| Molar Solubility (SLB.MOL) | <0.01 mol/L | pH 8 | (1) ACD |
| Molar Solubility (SLB.MOL) | <0.01 mol/L | pH 10 | (1) ACD |
| Molecular Weight (MW) | 492.73 | | (1) ACD |
| pKa (PKA) | 9.45+/-0.28 | Most Basic | (1) ACD |
| Vapor Pressure (VP) | 3.80E-20 Torr | 25.0 deg C | (1) ACD |

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software
Solaris V4.67 ((C) 1994-2005 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

7 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 135:300482 CA
 TITLE: Isolation of functionally active γ -secretase
 presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors
 INVENTOR(S): Roberts, Susan B.; Hendrick, Joseph P.; Vinitzky,
 Alexander; Lewis, Martin; Smith, David W.; Pak, Roger
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: G01N033-48
 CLASSIFICATION: 7-1 (Enzymes)
 Section cross-reference(s): 1, 9, 14
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001075435 | A2 | 20011011 | WO 2001-US10453 | 20010330 |
| WO 2001075435 | A3 | 20020808 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2405332 | AA | 20011011 | CA 2001-2405332 | 20010330 |
| US 2002025540 | A1 | 20020228 | US 2001-823153 | 20010330 |
| US 6713248 | B2 | 20040330 | | |
| EP 1305634 | A2 | 20030502 | EP 2001-922976 | 20010330 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2004505608 | T2 | 20040226 | JP 2001-572863 | 20010330 |
| US 2004121411 | A1 | 20040624 | US 2003-713981 | 20031114 |

Yours

PRIORITY APPLN. INFO.:

US 2000-194495P 20000403
US 2001-823153 20010330
WO 2001-US10453 20010330

ABSTRACT:

The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ -secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ -secretase. In one embodiment, the isolated γ -secretase protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β -amyloid precursor protein (β APP) by γ -secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ -cleaved β APP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ -cleaved β APP fragment, with substantially no cross-reactivity to uncleaved β APP or to other types of γ -cleaved β APP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the γ -cleaved β APP fragment. Detection of binding to the γ -cleaved β APP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

SUPPL. TERM: secretase gamma fluorescence detn amyloid precursor protein
cleavage; presenilin 1 gamma secretase complex purifn detn
INDEX TERM: Presenilins
ROLE: PRP (Properties); PUR (Purification or recovery); PREP
(Preparation)
(1, γ -secretase complexes; isolation of
functionally active γ -secretase presenilin 1
complex and fluorescence assay for γ -secretase
activity and inhibitors)
INDEX TERM: DNA sequences
(amyloid precursor protein-encoding; isolation of
functionally active γ -secretase presenilin 1
complex and fluorescence assay for γ -secretase
activity and inhibitors)
INDEX TERM: Allophycocyanins
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(cross-linked; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)
INDEX TERM: Rare earth complexes
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(cryptates; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)
INDEX TERM: UV lamps
(deuterium-tungsten lamp; isolation of functionally
active γ -secretase presenilin 1 complex and
fluorescence assay for γ -secretase activity and
inhibitors)
INDEX TERM: Laser induced fluorescence
(excitation; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)
INDEX TERM: Resonant energy transfer
(fluorescence; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)
INDEX TERM: Solubilization
Solubilizers
(in γ -secretase purification; isolation of functionally

active γ -secretase presenilin 1 complex and
fluorescence assay for γ -secretase activity and
inhibitors)

INDEX TERM: Drug screening
Epitopes
Fluorescence excitation
Fluorescence quenching
Fluorescent indicators
Immunoassay
Microsome
Post-translational processing
(isolation of functionally active γ -secretase
presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)

INDEX TERM: Amyloid precursor proteins
ROLE: ARG (Analytical reagent use); BPN (Biosynthetic
preparation); PRP (Properties); PUR (Purification or
recovery); THU (Therapeutic use); ANST (Analytical study);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(isolation of functionally active γ -secretase
presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)

INDEX TERM: Antibodies
ROLE: ARG (Analytical reagent use); BPN (Biosynthetic
preparation); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(isolation of functionally active γ -secretase
presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)

INDEX TERM: Rare earth complexes
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(isolation of functionally active γ -secretase
presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)

INDEX TERM: Antibodies
ROLE: ARG (Analytical reagent use); BPN (Biosynthetic
preparation); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(labeled; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)

INDEX TERM: Fluorescence excitation
(laser induced; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)

INDEX TERM: Proteins, specific or class
ROLE: PUR (Purification or recovery); PREP (Preparation)
(membrane, integral, solubilization of; isolation of
functionally active γ -secretase presenilin 1
complex and fluorescence assay for γ -secretase
activity and inhibitors)

INDEX TERM: Protein sequences
(of amyloid precursor protein; isolation of functionally
active γ -secretase presenilin 1 complex and
fluorescence assay for γ -secretase activity and
inhibitors)

INDEX TERM: Flash lamps
(xenon; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
assay for γ -secretase activity and inhibitors)

INDEX TERM: Amyloid
 ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (β-; isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence
 assay for γ-secretase activity and inhibitors)

INDEX TERM: 366522-28-3
 ROLE: PRP (Properties)
 (Unclaimed; isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence
 assay for γ-secretase activity and inhibitors)

INDEX TERM: 262412-30-6P 366520-86-7P
 ROLE: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence
 assay for γ-secretase activity and inhibitors)

INDEX TERM: 7440-33-7, Tungsten, analysis 7782-39-0, Deuterium, analysis
 ROLE: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
 (deuterium-tungsten lamp; isolation of functionally active γ-secretase presenilin 1 complex and
 fluorescence assay for γ-secretase activity and
 inhibitors)

INDEX TERM: 7440-63-3, Xenon, analysis
 ROLE: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
 (flash lamp; isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence
 assay for γ-secretase activity and inhibitors)

INDEX TERM: 338454-52-7DP, γ-Secretase, complexes with presenilin 1
 ROLE: ANT (Analyte); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (isolation of functionally active γ-secretase
 presenilin 1 complex and fluorescence assay for
 γ-secretase activity and inhibitors)

INDEX TERM: 338454-52-7, γ-Secretase
 ROLE: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (isolation of functionally active γ-secretase
 presenilin 1 complex and fluorescence assay for
 γ-secretase activity and inhibitors)

INDEX TERM: 81-88-9 91-64-5, Coumarin 2321-07-5, Fluorescein 6268-49-1 7440-53-1D, Europium, cryptates, biological studies 50402-56-7, EDANS 70281-37-7, Tetramethylrhodamine 146368-14-1 146368-16-3 247144-99-6 304014-12-8D, salts
 ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (isolation of functionally active γ-secretase
 presenilin 1 complex and fluorescence assay for
 γ-secretase activity and inhibitors)

INDEX TERM: 264902-77-4P, 3: PN: DE19849073 SEQID: 3 unclaimed DNA 366520-85-6P
 ROLE: BPN (Biosynthetic preparation); BUJ (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; isolation of functionally active

INDEX TERM: 76555-98-1
 ROLE: NUU (Other use, unclassified); USES (Uses)
 (solubilizer; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
 assay for γ -secretase activity and inhibitors)
 INDEX TERM: 366522-29-4 366801-12-9 366801-14-1
 ROLE: PRP (Properties)
 (unclaimed protein sequence; isolation of functionally
 active γ -secretase presenilin 1 complex and
 fluorescence assay for γ -secretase activity and
 inhibitors)
 INDEX TERM: 199164-91-5 366488-00-8 366488-01-9
 ROLE: PRP (Properties)
 (unclaimed sequence; isolation of functionally active
 γ -secretase presenilin 1 complex and fluorescence
 assay for γ -secretase activity and inhibitors)

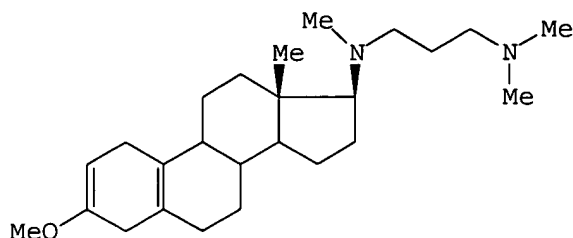
REFERENCE 2

ACCESSION NUMBER: 108:75714 CA
 TITLE: Steroids and their cyclic hydrocarbon analogs with
 amino-containing sidechains, useful as antidiabetic
 agents and inhibitors of phospholipase A2
 INVENTOR(S): Johnson, Roy A.; Bundy, Gordon L.; Youngdale, Gilbert
 A.; Morton, Douglas R.
 PATENT ASSIGNEE(S): Upjohn Co., USA
 SOURCE: PCT Int. Appl., 177 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C07J041-00
 SECONDARY: C07J043-00; A61K031-56; A61K031-58; C07C087-34;
 C07C087-455; C07D213-38; C07F009-24; C07F009-22;
 A61K031-13
 CLASSIFICATION: 32-3 (Steroids)
 Section cross-reference(s): 1, 2
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 8702367 | A2 | 19870423 | WO 1986-US2116 | 19861007 |
| WO 8702367 | A3 | 19880630 | | |
| W: JP, US, US | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| EP 243449 | A1 | 19871104 | EP 1986-906569 | 19861007 |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 63501217 | T2 | 19880512 | JP 1986-505710 | 19861007 |
| US 4917826 | A | 19900417 | US 1987-117851 | 19870616 |
| US 5196542 | A | 19930323 | US 1991-657721 | 19910220 |
| US 5145874 | A | 19920908 | US 1991-663037 | 19910225 |
| US 5187299 | A | 19930216 | US 1991-793486 | 19911113 |
| US 5274089 | A | 19931228 | US 1992-972693 | 19921106 |
| US 5334712 | A | 19940802 | US 1992-976751 | 19921116 |
| US 5373095 | A | 19941213 | US 1993-126153 | 19930923 |
| US 5621123 | A | 19970415 | US 1994-247169 | 19940520 |
| PRIORITY APPLN. INFO.: | | | US 1985-788995 | 19851018 |
| | | | US 1986-843120 | 19860324 |
| | | | WO 1986-US2116 | 19861007 |
| | | | US 1987-117851 | 19870616 |

US 1989-394396 19890815
 US 1991-657721 19910220
 US 1991-657729 19910220
 US 1991-793486 19911113
 US 1992-972693 19921106
 US 1992-976751 19921116

GRAPHIC IMAGE:



ABSTRACT:

A wide variety of steroids and nonsteroidal analogs bearing amino-containing sidechains were prepared for use as antidiabetic agents and in the treatment or prevention of phospholipase A2-mediated conditions. Reductive amination of estrone Me ether with Me₂N(CH₂)₃NH₂ and HCO₂H at 160-170° gave N-[3-(dimethylamino)propyl]-N-formyl-3-methoxyestra-1,3,5(10)-trien-17β-amine, which was reduced by LiAlH₄ in dioxane to the N-Me derivative. This underwent Birch reduction, followed by 3 recrystns. in Et₂O-MeCN, to give estradienamine derivative I. In the perfused guinea pig lung, I completely inhibited phospholipase A2 at 4 × 10⁻⁷ M.

SUPPL. TERM: amino steroid prepn antidiabetic phospholipase inhibitor;
 estranamine prepn antidiabetic phospholipase inhibitor

INDEX TERM: Antidiabetics and Hypoglycemics
 (amino steroids and analogs)

INDEX TERM: Steroids, preparation
 ROLE: SPN (Synthetic preparation); PREP (Preparation)
 (amino, preparation of, and analogs, as phospholipase A2
 inhibitors and antidiabetic agents)

INDEX TERM: 9001-84-7, Phospholipase A2
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (inhibitors of, amino-containing steroids and analogs as)

INDEX TERM: 53-44-1P 1434-85-1P, 17β-Hydroxy-5α-estran-3-
 one 1624-73-3P 5997-25-1P 30933-83-6P 40216-82-8P,
 Ornithine methyl ester dihydrochloride 57133-29-6P
 75950-19-5P 76555-98-1P 112646-79-4P 112647-70-8P
 112648-94-9P 112648-95-0P 112648-96-1P 112648-97-2P
 112648-98-3P 112648-99-4P 112649-00-0P 112649-01-1P
 112649-02-2P 112649-03-3P 112663-20-4P 112663-21-5P
 112663-22-6P 112663-31-7P 112663-33-9P 112663-34-0P
 112663-38-4P 112663-39-5P 112663-40-8P 112663-41-9P
 112663-42-0P 112663-44-2P 112663-45-3P 112663-46-4P
 112663-50-0P 112663-51-1P 112663-52-2P 112663-53-3P
 112663-54-4P 112663-55-5P 112663-56-6P 112663-57-7P
 112663-58-8P 112663-59-9P 112663-60-2P 112663-61-3P
 112663-62-4P 112663-63-5P 112663-67-9P 112693-14-8P
 112693-15-9P
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, in synthesis of phospholipase
 A2-inhibiting amino steroids and analogs)

INDEX TERM: 56-18-8P, 3,3'-Iminobis(propylamine) 26358-84-9P
 28336-31-4P

ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

| | | | | |
|-------------|--------------|--------------|--------------|---------------------|
| INDEX TERM: | 2640-80-4P | 4536-52-1P | 4991-61-1P | 4991-63-3P |
| | 5668-07-5P | 5997-25-1P | 6291-85-6P, | 3-Ethoxypropylamine |
| | 17630-26-1P | 17630-27-2P | 20432-64-8P | 32436-37-6P |
| | 57764-88-2P | 57764-89-3P | 59766-90-4P | 96148-91-3P |
| | 112646-53-4P | 112646-54-5P | 112646-55-6P | 112646-56-7P |
| | 112646-57-8P | 112646-58-9P | 112646-59-0P | 112646-60-3P |
| | 112646-62-5P | 112646-63-6P | 112646-65-8P | 112646-67-0P |
| | 112646-68-1P | 112646-69-2P | 112646-70-5P | 112646-71-6P |
| | 112646-72-7P | 112646-73-8P | 112646-74-9P | 112646-75-0P |
| | 112646-76-1P | 112646-77-2P | 112646-78-3P | 112646-79-4P |
| | 112646-80-7P | 112646-81-8P | 112646-82-9P | 112646-83-0P |
| | 112646-84-1P | 112646-85-2P | 112646-86-3P | 112646-87-4P |
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| | 112647-42-4P | 112647-43-5P | 112647-44-6P | 112647-45-7P |
| | 112647-46-8P | 112647-48-0P | 112647-49-1P | 112647-50-4P |
| | 112647-51-5P | 112647-52-6P | 112647-53-7P | 112647-54-8P |
| | 112647-55-9P | 112647-56-0P | 112647-57-1P | 112647-58-2P |
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| | 112647-67-3P | 112647-68-4P | 112647-69-5P | 112647-70-8P |
| | 112647-71-9P | 112647-72-0P | 112647-73-1P | 112647-74-2P |
| | 112647-75-3P | 112647-76-4P | 112647-77-5P | 112647-78-6P |
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| | 112648-16-5P | 112648-17-6P | 112648-18-7P | 112648-19-8P |
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| | 112648-32-5P | 112648-33-6P | 112648-34-7P | 112648-35-8P |
| | 112648-36-9P | 112648-37-0P | 112648-38-1P | 112648-39-2P |
| | 112648-40-5P | 112648-41-6P | 112648-42-7P | 112648-43-8P |
| | 112648-44-9P | 112648-45-0P | 112648-46-1P | 112648-47-2P |
| | 112648-48-3P | 112648-49-4P | 112648-50-7P | 112648-51-8P |
| | 112648-52-9P | 112648-53-0P | 112648-54-1P | 112648-55-2P |
| | 112648-56-3P | 112648-57-4P | 112648-58-5P | 112648-59-6P |
| | 112648-60-9P | 112648-61-0P | 112648-62-1P | 112648-63-2P |
| | 112648-64-3P | 112648-65-4P | 112648-66-5P | 112648-67-6P |
| | 112648-68-7P | 112648-69-8P | 112648-70-1P | 112648-71-2P |
| | 112648-72-3P | 112648-73-4P | 112648-74-5P | 112648-75-6P |
| | 112648-76-7P | 112648-77-8P | 112648-78-9P | 112648-79-0P |

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as phospholipase A2 inhibitor and/or
antidiabetic agent)

| | | | | |
|-------------|--------------|--------------|--------------|--------------|
| INDEX TERM: | 112648-80-3P | 112648-81-4P | 112648-82-5P | 112648-83-6P |
| | 112648-84-7P | 112648-85-8P | 112648-86-9P | 112648-87-0P |
| | 112648-88-1P | 112648-89-2P | 112648-90-5P | 112648-91-6P |
| | 112648-92-7P | 112648-93-8P | 112649-04-4P | 112649-05-5P |
| | 112649-06-6P | 112663-15-7P | 112663-16-8P | 112663-17-9P |
| | 112663-18-0P | 112663-19-1P | 112663-23-7P | 112663-24-8P |
| | 112663-25-9P | 112663-26-0P | 112663-27-1P | 112663-28-2P |
| | 112663-29-3P | 112663-30-6P | 112663-32-8P | 112663-35-1P |
| | 112663-36-2P | 112663-47-5P | 112663-48-6P | 112663-49-7P |
| | 112663-64-6P | 112663-65-7P | 112663-66-8P | 112710-67-5P |
| | 112710-68-6P | 112710-69-7P | 112711-11-2P | 112711-12-3P |

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as phospholipase A2 inhibitor and/or
antidiabetic agent)

| | | | |
|-------------|--|---------------------------------------|--|
| INDEX TERM: | 50-28-2, reactions | 51-67-2, Tyramine | 53-16-7, Estrone, |
| | reactions | 53-41-8 | 53-43-0, 3 β -Hydroxy-5-androsten- |
| | 17-one | 53-45-2, Estra-1,3,5(10)-trien-17-one | 64-04-0, |
| | Phenethylamine | 64-18-6, reactions | 71-44-3, Spermine |
| | 75-07-0, reactions | 79-04-9 | 81-25-4 |
| | 2-Chlorobenzylamine | 90-42-6, 2-Cyclohexyl cyclohexanone | 89-97-4, |
| | 91-00-9, Aminodiphenylmethane | 92-68-2, | |
| | 4-Cyclohexylcyclohexanone | 95-00-1, 2,4-Dichlorobenzylamine | |
| | 96-32-2, Methyl bromoacetate | 100-46-9, reactions | |
| | 100-52-7, reactions | 102-49-8, 3,4-Dichlorobenzylamine | |
| | 104-53-0, Hydrocinnamaldehyde | 104-86-9, | |
| | 4-Chlorobenzylamine | 104-88-1, 4-Chlorobenzaldehyde, | |
| | reactions | 105-39-5, Ethyl chloroacetate | 107-13-1, |
| | reactions | 107-85-7, Isoamylamine | 108-00-9, |
| | unsym-Dimethyl-ethylenediamine | 108-31-6, reactions | |
| | 108-94-1, reactions | 109-01-3, N-Methylpiperazine | |
| | 109-55-7, 3-Dimethylaminopropylamine | 109-64-8, | |
| | 1,3-Dibromopropane | 109-76-2, 1,3-Propanediamine | |
| | 110-13-4, 2,5-Hexanedione | 110-60-1, 1,4-Diaminobutane | |
| | 111-40-0 | 123-00-2, 3-Morpholinopropylamine | 123-38-6, |
| | reactions | 124-09-4, reactions | 124-13-0, Octylaldehyde |
| | 124-20-9, Spermidine | 124-25-4, Tetradecyl aldehyde | |
| | 138-14-7 | 140-75-0, 4-Fluorobenzylamine | 140-80-7, |
| | 2-Amino-5-diethylaminopentane | 156-87-6 | 327-92-4, |
| | 1,5-Difluoro-2,4-dinitrobenzene | 333-93-7, | |
| | 1,4-Diaminobutane dihydrochloride | 373-44-4, | |
| | 1,8-Octanediamine | 462-94-2, 1,5-Diaminopentane | 502-72-7, |
| | Cyclopentadecanone | 506-59-2, Dimethylamine hydrochloride | |
| | 566-88-1, 5 α -Cholestan-3-one | 590-86-3, | |
| | Isovaleraldehyde | 593-51-1, Methylamine hydrochloride | |
| | 598-21-0, Bromoacetyl bromide | 617-89-0, | |
| | 2-Aminomethyl-furan | 646-25-3, 1,10-Decanediamine | |
| | 700-58-3, 2-Adamantanone | 766-39-2, 2,3-Dimethylmaleic | |
| | anhydride | 814-68-6, Acryloyl chloride | 830-13-7, |
| | Cyclododecanone | 929-06-6, 2-(2-Aminoethoxy)ethanol | |
| | 963-74-6, 5 α -Androstan-17-one | 1035-77-4, Estradiol | |
| | 3-methyl ether | 1624-62-0, Estrone methyl ether | 1755-52-8 |
| | 2038-03-1, 2-Morpholinoethylamine | 2393-23-9, | |
| | 4-Methoxybenzylamine | 2524-64-3, Diphenyl chlorophosphate | |
| | 2706-56-1, 2-(2-Aminoethyl)pyridine | 2740-83-2, | |
| | 3-(Trifluoromethyl)benzylamine | 3029-19-4, | |
| | 1-Pyrenecarboxaldehyde | 3048-01-9 | 3179-63-3 |
| | 4-(Trifluoromethyl)benzylamine | 3731-51-9, | 3300-51-4, |
| | 2-(Aminomethyl)pyridine | 3731-52-0, 3-(Aminomethyl)pyridine | |

3731-53-1, 4-(Aminomethyl)pyridine 4048-33-3,
 6-Amino-1-hexanol 4097-89-6, Tris-(2-aminoethyl)amine
 4894-75-1 5036-48-6 5104-49-4, Flurbiprofen 5538-95-4,
 N-Dodecyl-1,3-propanediamine 5625-80-9 5680-79-5,
 Glycine methyl ester hydrochloride 5993-91-9 6211-16-1
 6384-10-7, Ornithine methyl ester 6711-48-4 7149-10-2
 7152-51-4 7209-38-3, 1,4-Bis(3-aminopropyl)piperazine
 7663-77-6, 1-(3-Aminopropyl)-2-pyrrolidinone 10025-87-3
 10517-44-9 13258-63-4, 4-(2-Aminoethyl)pyridine
 14210-25-4 19475-35-5 21370-71-8, trans-1-Decalone
 27757-85-3, 2-Thiophenemethylamine 28143-91-1 29602-39-9
 30525-89-4, Paraformaldehyde 31239-17-5,
 5 α -Androstan-17 β -amine 34015-48-0, Lysine
 methyl ester dihydrochloride 35303-76-5,
 4-(2-Aminoethyl)benzenesulfonamide 40226-15-1 42014-51-7
 49783-80-4 55757-60-3 56183-69-8, Diethyl
 phosphorohydrazidate 69225-59-8 75659-75-5 83732-75-6,
 2-(2-Aminoethyl)-1-methylpyrrole 85666-15-5 112663-37-3
 112663-43-1

ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, in synthesis of phospholipase A2-inhibiting
 amino steroids and analogs)

REFERENCE 3

ACCESSION NUMBER: 104:187118 CA
 TITLE: Fixed steroids
 INVENTOR(S): Itagaki, Koji; Ito, Takeshi; Ando, Kyoto
 PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
 CODEN: JKXXAF

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 INT. PATENT CLASSIF.:

MAIN: C08F008-00
 CLASSIFICATION: 35-8 (Chemistry of Synthetic High Polymers)
 Section cross-reference(s): 32, 80

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 60133005 | A2 | 19850716 | JP 1983-241342 | 19831221 |
| PRIORITY APPLN. INFO.: | | | JP 1983-241342 | 19831221 |

ABSTRACT:

Products useful as carriers in affinity chromatog. are prepared by amidation of carboxylated steroids with polyalkylenepolyamines and reaction of the amides with insol. matrix polymers having amine-reactive groups. Thus, heating 20 g Et cholate with 100 g Me₂N(CH₂)₃NH₂ 16 h at 140° gave 21.1 g amide. Heating 19.4 g amide and 5 g chloromethylated styrene-divinylbenzene polymer in 1:1 dioxane-MeOH for 16 h at 70° gave 10.3 g fixed steroid (ion exchange volume 1.08 mequiv/g dry resin).

SUPPL. TERM: styrene copolymer matrix chromatog; cholic amide fixation chromatog; affinity chromatog steroid fixation; amide steroid carrier chromatog; dimethylpropanediamine reaction cholic acid

INDEX TERM: Chromatography, column and liquid
 (affinity, stationary phases for, fixed steroids as)

INDEX TERM: 9003-70-7D, chloromethylated, reaction products with steroid aminoamides 76555-98-1D, reaction products with chloromethylated styrene copolymers

ROLE: USES (Uses)

(carriers in affinity chromatog.)

REFERENCE 4

ACCESSION NUMBER: 99:2687 CA
TITLE: Sulfo betaine derivatives of bile acids: nondenaturing
surfactants for membrane biochemistry
AUTHOR(S): Hjelmeland, Leonard M.; Nebert, Daniel W.; Osborne,
James C., Jr.
CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum.
Dev., Bethesda, MD, 20205, USA
SOURCE: Analytical Biochemistry (1983), 130(1), 72-82
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-10 (Biochemical Methods)
Section cross-reference(s): 32, 46

ABSTRACT:

The syntheses of 4 new sulfo betaine derivs. of bile salts are presented, along with a general set of criteria for useful detergents in membrane biochem. Phys. properties including the critical micelle concentration, aggregation number, partial sp. volume, critical micellar temperature, UV-visible spectrum, and CD spectrum were examined for the new compds. To examine the interaction of this class of compds. with macromols., CHAPS was further studied. CD spectra of apolipoprotein C-III2 were measured in the presence of varying concns. of CHAPS to determine the effect of this compound on secondary structure. Gel-exclusion chromatog. and sedimentation equilibrium studies of cytochrome P 450 in the presence of CHAPS was also performed to establish the ability of this detergent to disaggregate cytochrome P 450 to a monomeric/dimeric state.

SUPPL. TERM: detergent prepn bile acid deriv; sulfo betaine deriv
zwitterionic surfactant
INDEX TERM: Detergents
(preparation of nondenaturing, for membrane biochem.)
INDEX TERM: Bile acids
ROLE: ANST (Analytical study)
(sulfo betaine derivs., as nondenaturing detergents)
INDEX TERM: Betaines
ROLE: ANST (Analytical study)
(sulfo-, cholic acid derivs., as nondenaturing detergents)
INDEX TERM: 9035-51-2, biological studies
ROLE: BIOL (Biological study)
(disaggregation of, by sulfo betaine derivs. of bile acids)
INDEX TERM: 81-25-4 83-44-3
ROLE: ANST (Analytical study)
(mixed anhydride preparation from)
INDEX TERM: 76555-98-1P 85954-19-4P
ROLE: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of)
INDEX TERM: 75621-03-3P 82473-24-3P 85964-38-1P 85964-39-2P
ROLE: PREP (Preparation)
(preparation and characterization of, as nondenaturing detergent for membrane biochem.)
INDEX TERM: 85954-17-2P 85954-18-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with dimethylaminopropylamine)
INDEX TERM: 109-55-7 6711-48-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with cholic acid anhydride)

REFERENCE 5

ACCESSION NUMBER: 97:52173 CA
TITLE: Nondenaturing zwitterionic detergents for membrane
biochemistry
INVENTOR(S): Hjelmeland, Leonard
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U. S. Pat. Appl., 47 pp. Avail. NTIS Order No.
PAT-APPL-6-294 203
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
CLASSIFICATION: 9-10 (Biochemical Methods)
Section cross-reference(s): 46
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 294203 | A0 | 19820409 | US 1981-294203 | 19810819 |
| US 4372888 | A | 19830208 | | |
| US 181465 | A0 | 19810327 | US 1980-181465 | 19800826 |
| WO 8300694 | A1 | 19830303 | WO 1982-US1123 | 19820819 |
| W: JP | | | | |
| RW: AT, BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| JP 58501279 | T2 | 19830804 | JP 1982-502842 | 19820819 |
| EP 85717 | A1 | 19830817 | EP 1982-902934 | 19820819 |
| EP 85717 | B1 | 19861029 | | |
| R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE | | | | |
| CA 1179326 | A1 | 19841211 | CA 1982-409779 | 19820819 |
| AT 23166 | E | 19861115 | AT 1982-902934 | 19820819 |
| PRIORITY APPLN. INFO.: | | | US 1980-181465 | 19800826 |
| | | | US 1981-294203 | 19810819 |
| | | | EP 1982-902934 | 19820819 |
| | | | WO 1982-US1123 | 19820819 |

ABSTRACT:

Preparation of 2 nondenaturing zwitterionic detergents, 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS) and 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), is described for solubilization of membrane proteins. CHAPSO was 2-fold more effective in solubilizing active opiate receptors than CHAPS.

SUPPL. TERM: membrane protein solubilization zwitterionic detergent
INDEX TERM: Receptors
ROLE: PROC (Process)
(for opiates, solubilization of, nondenaturing
zwitterionic detergents for)
INDEX TERM: Membrane, biological
(protein solubilization of, nondenaturing zwitterionic
detergents for)
INDEX TERM: Opiates and Opioids
ROLE: ANST (Analytical study)
(receptors for, solubilization of, nondenaturing
zwitterionic detergents for)
INDEX TERM: Proteins
ROLE: PROC (Process)
(solubilization of, of membranes, nonnaturing
zwitterionic detergents for)
INDEX TERM: Detergents
(zwitterionic, for membrane protein solubilization)
INDEX TERM: 76555-98-1P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reactions of, with propanesultone or sodium chlorohydroxypropanesulfonate)
 INDEX TERM: 82473-24-3P
 ROLE: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as detergent for membrane protein solubilization)
 INDEX TERM: 75621-03-3P
 ROLE: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as detergent for solubilization of membrane proteins)
 INDEX TERM: 109-55-7
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with cholic acid)
 INDEX TERM: 81-25-4
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with dimethylaminopropylamine)
 INDEX TERM: 126-83-0
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with dimethylaminopropylcholamide)
 INDEX TERM: 1120-71-4
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with dimethylpropylcholamide)

REFERENCE 6

ACCESSION NUMBER: 95:38693 CA
 TITLE: Nondenaturing zwitterionic detergents for membrane biochemistry
 INVENTOR(S): Hjelmeland, Leonard M.
 PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA
 SOURCE: U. S. Pat. Appl., 22 pp. Avail. NTIS Order No. PAT-APPL-181 465.
 CODEN: XAXXAV
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 CLASSIFICATION: 9-13 (Biochemical Methods)
 Section cross-reference(s): 32
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|----------|-----------------|----------|
| US 181465 | A0 | 19810327 | US 1980-181465 | 19800826 |
| CA 1173823 | A1 | 19840904 | CA 1981-382720 | 19810728 |
| EP 46523 | A1 | 19820303 | EP 1981-106105 | 19810804 |
| EP 46523 | B1 | 19840725 | | |
| R: BE, CH, DE, FR, GB | | | | |
| US 294203 | A0 | 19820409 | US 1981-294203 | 19810819 |
| US 4372888 | A | 19830208 | | |
| JP 57073095 | A2 | 19820507 | JP 1981-132668 | 19810826 |
| JP 03002877 | B4 | 19910117 | | |

PRIORITY APPLN. INFO.: US 1980-181465 19800826

ABSTRACT:

Preparation of zwitterionic detergents, which are a combination of a bile salt hydrophobic group and a sulfobetaine-type polar group, is described for solubilizing membrane proteins in a nondenatured state. 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate (I) preparation is described. The Et₃NH⁺ salt of cholic acid was formed in THF, then ethylchloroformate was added to precipitate Et₃NHCl, which was removed from the mixed anhydride by filtration. The mixed anhydride reacted with 3-dimethylaminopropylamine to

form N-(3-dimethylaminopropyl)cholamide (II), EtOH, and CO₂. In the final step, the tertiary amine group of II reacted with propane sultone to give the sulfobetaine, I. The yield was 75-80% theor., and the purity of I was >95% as judged by TLC.

SUPPL. TERM: membrane protein solubilization zwitterionic detergent;
cholamidopropyltrimethylammoniopropanesulfonate membrane
protein; cholate sulfobetaine deriv detergent

INDEX TERM: Detergents
(for membrane proteins solubilization, nondenaturing
zwitterionic)

INDEX TERM: Proteins
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(of membranes, solubilization of, nondenaturation
zwitterionic detergents preparation for)

INDEX TERM: Cell membrane
(proteins of, solubilization of, nondenaturing
zwitterionic detergents preparation for)

INDEX TERM: Solubilizers
(zwitterionic nondenaturing detergent, for membrane
proteins)

INDEX TERM: 78327-01-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with 3-dimethylaminopropylamine)

INDEX TERM: 1120-71-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with
dimethylaminopropylcholamide)

INDEX TERM: 76555-98-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with propanesultone)

INDEX TERM: 75621-03-3P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as nondenaturing detergent for membrane
protein solubilization)

INDEX TERM: 121-44-8, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cholate)

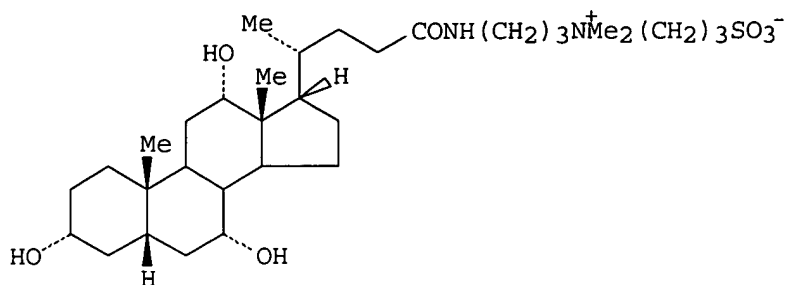
INDEX TERM: 81-25-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triethylamine)

INDEX TERM: 109-55-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triethylammonium cholate)

REFERENCE 7

ACCESSION NUMBER: 94:79812 CA
TITLE: A nondenaturing zwitterionic detergent for membrane
biochemistry: Design and synthesis
AUTHOR(S): Hjelmeland, Leonard M.
CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum.
Dev., Bethesda, MD, 20205, USA
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America (1980), 77(11), 6368-70
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-13 (Biochemical Methods)
Section cross-reference(s): 6

GRAPHIC IMAGE:



I

ABSTRACT:

The synthesis and evaluation of a new detergent that is a zwitterionic derivative (I) of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

SUPPL. TERM: CHAPS prepn microsome solubilization;
cholamidopropyldimethylaminopropanesulfonate prepn microsome
solubilization; surfactant prepn microsome solubilization

INDEX TERM: Surfactants
(CHAPS, preparation and membrane-solubilizing properties of)

INDEX TERM: Microsome
(solubilization of, by nondenaturing detergent)

INDEX TERM: 75621-03-3P
ROLE: PREP (Preparation)
(preparation and membrane-solubilizing properties of)

INDEX TERM: 76555-98-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and reaction with propanesultone)

INDEX TERM: 109-55-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cholic acid)

INDEX TERM: 81-25-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dimethylaminopropylamine)

INDEX TERM: 1120-71-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dimethylaminopropylcholamide)

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